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# ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY

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VOL. 50

DECEMBER, 1941

No. 4

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LXXIII

## LEONARDO DA VINCI'S CONTRIBUTION TO LARYNGOLOGY, RHINOLOGY AND PHONETICS\*

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In turning back in time, approximately four hundred years, for we are dealing with a period from 1452-1519, to comment on the accomplishments of one man, the data must be such that it is the very source of information and not hearsay. Fortunately, in this instance, the original note books of Leonardo da Vinci have been reassembled, and it is these notes — facsimile copies — on which the following remarks are based.

Leonardo recorded a great many of his thoughts, plans and anatomical drawings in note books or note leaves. His principal heir and executor who swore that "in his comings and goings, he will say and do nothing contrary" to the Will, — received all of these note books. This young man, Francesco Melzi, was bequeathed by Leonardo, "each and all of the books which the said testator has at present, and other instruments and portraits connected with his art and occupation as painter." These note books were carefully preserved and treasured by Melzi. Later they became the property of his son and eventually they were inherited by the grandson, who recognized

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\*Read before the Section on Otolaryngology of the College of Physicians of Philadelphia, November 19th, 1941.



Fig. 1. This photograph is a copy of a self portrait of Leonardo da Vinci, and is the only known existing one. This painting is in the Royal Palace in Turin, Italy.

There is an old tradition, that couples his name with a picture of an Archangel painted by a pupil of Verrocchio but for some time attributed to Botticelli. However, this was a painting made during his youth. (Vallentin, A. Viking Press, Inc., 1938, pp. 31.)

their pecuniary value, and disposed of individual books and even leaves to the highest bidder. Some of these notes, especially the ones dealing with the anatomical studies, came into the possession of Charles II, King of Spain and Francis I, King of France. They were placed in their individual archives, where they became lost. Eventually, a number of these note books have been recovered or "rediscovered" and have found their way into the Library at Windsor Castle, England. These notes in the Windsor Castle Library were assembled, in part, by Giovanni Piumati and published by Theodor Sabacknikoff in French in 1898 in two folio volumes entitled, "Dell' Anatomia." A more complete assembly of these notes of the Windsor Library collection of Leonardo's manuscripts was made by Vangensten, Fonahn and Hopstock of Christiania in 1911-1916, and



resulted in six folio volumes. These volumes were entitled, "Quaderni D'Anatomia." These facsimile volumes are in the original Italian of Leonardo's times but with many interpolations. The Quaderni D'Anatomia consist of transpositions of the original notes and translations into modern Italian, English and German. It is interesting to note that Leonardo was left-handed and that he wrote from right to left. With a mirror or a photographic positive of the negative reversed, his writings are easily read.

There is another publication that contains Leonardo's manuscripts on philosophy, engineering, mathematics, aeronautics and some few anatomical drawings. These eight folio volumes are entitled the "Codex Atlanticus," and were published in facsimile for the Ambrosiana Library, in Milan, by Ulrico Hoepli, 1894-1904. It is in these volumes that his notes on the flying apparatus are given in detail, various types of cannon, directions how to use the mandrils in reaming the bores, and especially the description of a spherical projectile filled with gunpowder and balls. "The centre ball bursts and scatters the rest within a period of time, no longer than an Ave Maria." (Codex Atlanticus, 24 Recto A; 308 Recto 8; 308 Recto B, Verso A.)

The description of the famed armored car shooting flames in all directions, undoubtedly, was part of these drawings on military engineering and ordnance but became separated from them so that the original is in the British Museum and the others are in the Windsor Castle Library. In the first instance the precursor of the deadly shrapnel and in the latter — the present military tank. Here, also he suggests the importance of the use of infantry in conjunction with this battle car.

Leonardo's insatiable desire for knowledge led him to much deeper researches than the mere study of the bones and surface anatomy. However, the Galenic aberrations and prejudices were so deeply rooted, that Leonardo, even with his keen observations, was befuddled. Galen died at the end of the second century.

In 1543, twenty-four years after Leonardo died, Andreas Vesalius in his "De Corporis Humani Fabrica" showed the various fallacies of the anatomical drawings of Galen and that they were mostly anatomical studies of apes. This caused such a disturbance, that the theory was advanced that in the eight to nine hundred years which had elapsed since Galen's time, the human body had changed.

McMurrich in his volume on Leonardo da Vinci, the Anatomist, shows the outstanding merits of Leonardo's anatomical studies but



Fig. 2. This is self-explanatory and gives the title pages of the facsimile copies in which Leonardo's notes are embodied.

Through the courtesy of Dr. A. Malloch, Librarian of the New York Academy of Medicine, these facsimile volumes were placed at my disposal.

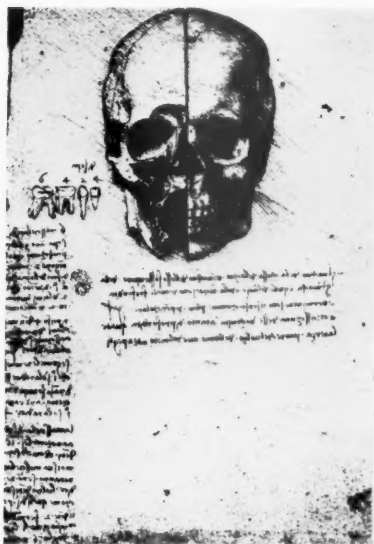


Fig. 3. Split skull. Frontal and maxillary sinuses exposed. Anterior wall has been removed showing the floor of the sinuses on the right side. There is a septum of bone just beyond the median line. This may be the left frontal or an ethmoid cell.

The frontal eminence is seen on the left side and the supraorbital notch. The frontoparietal suture is seen.

The right nasal bone has been removed. Lacrimal duct has been exposed. Maxillary sinus with floor lower than nasal floor. Interior of the sinus is well exposed. The upper alveolar ridge has been removed, also the anterior part of the mandible has been removed. The teeth are described and grouped according to function. Malar bone has been resected to show the interior of the maxillary sinus. Zygomatic arch is partially shown.

Leonardo was the first anatomist to make vertical and horizontal sections of the human body. (*Dell' Anatomia*, Fogli B, 41 Verso.)

also their weaknesses. Nevertheless, Leonardo may be considered the St. John preceding the "de Fabrica" of Vesalius.

If Leonardo's anatomical drawings had been published during his lifetime (1452-1519) that is, during the first decades of the sixteenth century, it would have revolutionized the study of anatomy, physiology and in general advanced the progress of medicine and surgery tremendously.



Fig. 4. The anterior and lateral wall of the right maxillary sinus has been removed in the lower drawing. A comparison of the orbit and maxillary sinus is made. The floor of the maxillary reveals the intrusion of the roots of the teeth. Zygomatic arch and external auditory canal are seen. Frontal eminence and frontal protuberance, including the squamous portion of the temporal bone and also the mastoid process, are seen. Sutures are plainly indicated.

The occipital bone rests on a block and thus the skull is in a more life-like position.

This drawing was made with a silver pencil and even in the facsimile copy it appears like a copper engraving. (Dell' Anatomia, Fogli B, 40 Verso.)

It is only within our own time that his anatomical studies have become known, specifically, the first edition of facsimile copies of his drawings having been published in 1898.

The painting, the *Mona Lisa*, in the opinion of most critics, has never been surpassed by any artist, but his anatomical and engineering studies indicated that most of his thoughts were of a scientific nature.

Painter, sculptor, architect, engineer and anatomist, a combination that makes us pause and contemplate. Surely here is one of the greatest men that has ever lived.

In the *Quaderni D'Anatomia*, Vol. 1, Folio 13, Verso (paragraphs 14 and 15) he says: "And you who say that it is better to see the dissection than such drawings, you would speak well, if it were possible, to see all these things, which are demonstrated in such drawings in a single specimen in which you, with all your genius—will not see and will not obtain knowledge except of a few veins; for having the true and full knowledge of which I have dissected, more than ten human bodies, destroying all other organs, consuming with very minutest particles all flesh, which surrounded these veins, without making them bloody except with insensible sanguinification of the capillary veins; and one body did not suffice for so long a time, so that it was necessary to proceed by degrees with so many bodies that the complete knowledge might be completed, which I twice repeated in order to see the difference."

"And if you have love for such matter, you will perhaps be impeded by the stomach, and if that does not impede you, you will perhaps be impeded by the fear of living in the night hours in company of such quartered and flayed corpses, fearful to look at, and if this does not impede you, you will perhaps lack good draughtsmanship, which belongs to such demonstration, and, if you have the draughtmanship it will not be accomplished by the perspective, and if it is accompanied, you will lack the order of the geometrical demonstrations and the order of the calculation of the forces and power of the muscles; and, perhaps you will lack patience, so that you will not be diligent. As to whether all these things have been in me or not, the 100 and 20 books composed by me, will furnish sentence Yes or No, in which I have not been impeded by avarice or negligence, but only by time. Vale!"

In the description of the drawing in Figure 4, Leonardo states, "that the maxillary sinus has a capacity equal to the orbit and that it contains a humor that nourishes the roots of the teeth. It receives nerves that descend from the brain passing through the cribriform



Fig. 5. Section of the body showing relation of the gullet and airways, lungs, heart, situs spiritualis, stomach, belly, umbilicus, bladder, spleen and kidney.

The spiritualis is located in the thoracic cavity, near the heart. (*Quaderni D'Anatomia*, Vol. 5, Fol. 20, Verso.)

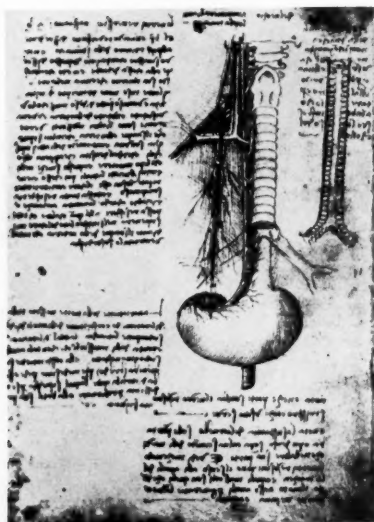


Fig. 6. The upper cervical vertebrae, larynx, trachea and its bifurcation with right and left bronchi, are shown.

Lower esophagus, stomach, vascular arborizations on the lesser curvature, the fundus, greater curvature, pylorus and duodenum, are shown.

The muscle fibres of the stomach wall are plainly seen.

At the right of this drawing, the trachea is shown and its bifurcation. The absence of the rings of the trachea is indicated. This was probably not a human trachea for there are 28 rings. The vagus is well demonstrated and also the recurrent laryngeal nerve. The different angle of the bifurcation of the trachea into the right and left bronchi, is shown. (Dell' Anatomia, Fogli B, Verso 33.)

plate of the ethmoid, which discharges into the nose the superfluity of the humor of the head." "The bony nasolacrimal duct through which the tears ascend from the heart to the eye passing by way of the nasal canal," is described. "Who would believe that so small a space [meaning the eye] could contain the images of the universe. O, Mighty Process! What skill can avail to penetrate a nature such as thine? What tongue can unfold so great a wonder? Truly none! This it is that leads human discourse to the consideration of things Divine." (Quaderni D'Anatomia, Vol. I, Folio 10.)

McMurrich states that "credit for the first representation of the cranial sinuses, excepting the mastoid, belongs to Leonardo.

They were unknown to Galen and therefore to Avicenna, A. D. 980-1038. Vesalius mentions them." The description of this anatomical dissection was probably made by Leonardo around 1489. It resembles a copper engraving for it was made with a fine silver pencil.

These anatomical drawings were to be included in the "book on the human form." There is no record that this book was published, or if it was, it may have suffered the fate of his "Trattato de Vocie" which was to be delivered on December 14th, 1514 by the Papal Chamberlain, Battista dell' Aquila, to Pope Leo X. This manuscript with splendid drawings disappeared, and only a few preparatory notes and sketches, bear witness to this effort. (Codex Atlanticus 287 Recto.)

The maxillary sinus had to wait until 1651 for its full description by Highmore, who called it the antrum, a term previously used by Laurentius.

The mastoid sinus was observed by Ingrassius in 1603.

As an engineer, Leonardo stands high for his plans to drain the Pontine Marshes, his various architectural plans, from palaces to stables to house 125 horses, and especially his knowledge and understanding, as repeatedly demonstrated, of the "strength of materials," but he failed to grasp the fundamental reason for the accessory sinuses; that is, that they lessen the weight of the face and skull and by their conformation strengthen the entire structure.

Figure 5 is taken from a page in the Quaderni D'Anatomia, Vol. 5, Folio 20 Verso, and shows the relationship of the esophagus, trachea and the various viscera of the thorax and abdomen. It is on a page with geometrical problems and other calculations. The important viscera are labelled and somewhere within the chest cavity, near the heart, Leonardo indicates the *situs spiritualis*.

Elsewhere (Quaderni D'Anatomia, Vol. 4, Folio 10 Recto, paragraph 12) he says, "the rest of the definition of the Soul I leave to the mind of the Monks,—*'padri de' popoli'*,—who by inspiration, know all things."

Leonardo's description of the tonsils is that they arise in the opposite parts of the base of the tongue like two cushions interposed between the bone of the maxilla and the base of the tongue, that it may on one side receive the lateral globosity of the convex part which arises on the tongue when it curves itself, and that it may,



Fig. 7.

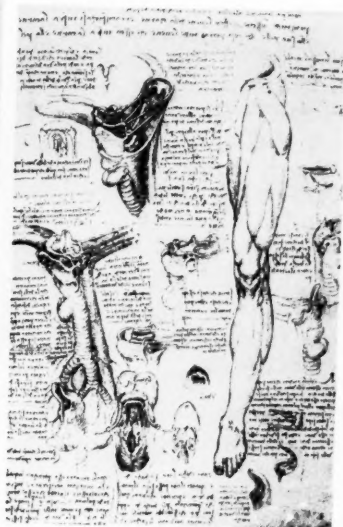


Fig. 8.

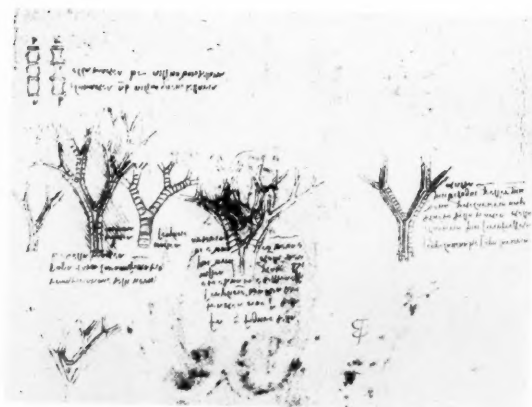


Fig. 9.



Fig. 7. The muscles at the root of the tongue are shown and appear to be the fibres of *m. genioglossus* and *m. geniohyoideus*. Also the tonsil labelled "ama . . ." (the last characters not being clearly defined) and the tongue labelled "lingua," are described in the script to the right.

Veins of the upper extremity and the large veins and arteries of the neck, including the aortic arch, are shown.

There is a very comprehensive sketch of the larynx showing thyroid cartilage, thyroid notch, superior cornu; articulating with the superior cornu of the hyoid bone and above the body of the hyoid is seen, and also the edge of the epiglottis.

The thyrohyoid membrane and what appears to be a suggested sketch of the glottic chink, are shown in the right central part of the drawing.

The cricoid cartilage is represented as about the size of the first ring of the trachea. The first ring of the trachea and definitely a *pomum adami*, are shown. (Quaderni D'Anatomia, Vol. IV, Fol. 9 Verso.)

Fig. 8. Here are shown many sketches of the tongue, hyoid bone, uvula and soft palate, thyroid cartilage, epiglottis, trachea, bifurcation, etc.

The laryngeal introitus and the epiglottis and the relation to the hyoid bone, are included.

The thyroid gland is shown in many sketches.

In the upper right part of the illustration, there is shown what appears to be the glottic chink, and in the lower part, next to the leg drawing, there will be seen the arytenoids. The vocal cords are not described. The description in the text is very vague. (Dell' Anatomia, Fogli A, Recto 3.)

Fig. 9. There are several drawings of the trachea and bronchi, with ramifications to the third subdivisions. The absence of the posterior part of the cartilaginous rings of the trachea and the bronchi is shown.

The right upper lobe bronchus is not shown in any of these sketches.

The right and left main bronchi are shown to be about equal in size and angle of bifurcation.

There seems to be a shadowy sketch of an inverted torso in the central part of the drawing.

The accompanying blood vessels of the bronchi are shown. (Quaderni D'Anatomia, Vol. 2, Fol. 2 Recto.)

with the convex part, clean the angles of the maxilla of the food at the lateral parts of the base of the tongue. (Fig. 7.)

In Figure 9 the trachea and the bronchi with ramification to the third subdivision, are shown. The upper lobe bronchus is not shown in any of these drawings. There are shown the accompanying vein and artery. The word "trachea" denotes trachea and also bronchi and bronchioles as far as they can be followed. In one of the dissections, he notes that he found in the bronchus, a nut-like encrustation, "in the interior were dust and aqueous humor"—possibly a broncho-lith.

Leonardo discusses at length the movements of the tongue and phonetics and other things in the manuscript in Figure 10.

He states that the principal movements of the tongue are seven, that is (paragraph 7): "extension and retraction and attraction, thickening, shortening, dilation and straightening. Of these movements, three are compound ones, because one of these cannot be generated without another being generated to the first one, from necessity. And this is the first with the second that it extends and retracts itself . . . and similar things happen in the third and fourth movement contrary to the two first, i.e., to thicken and shorten the tongue. Follow the fifth and sixth movements which makes its third movement composed of three movements, i.e., dilation, straightening and shortening. . . . The tongue [paragraph 7] works in pronunciation and articulation of the syllables, the composers of all words. Moreover, this tongue is acting in the necessary revolution of the masticated food." The illustration of the movement of the tongue is of a woodpecker (paragraph 9). In the lower right corner of this drawing, he states that "this discourse does not belong here," (paragraph 11). "It is proved [paragraph 3] how all the vowels are pronounced with the back part of the movable palate, which covers the epiglottis; and furthermore such pronunciation comes from the position of the lips by means of which passage is given to the outstreaming air which carries with itself the created sound of the voice; which sound even though the lips are closed, streams through the nostrils . . . through such experiment you may with certainty conclude that the 'trachea' does not create any sound of vocal letters but its office only extends to the creation of the aforesaid voice and especially in a, o, u." The epiglottis was the common medieval term for the larynx. What is now termed the epiglottis, was known as the *linguella* or *coopertorium*. The glottic chink was termed the *fistola* by Leonardo.

In the Quaderni D'Anatomia, Vol. 4, Folio 10 Verso, Leonardo describes his conception of the production of the human voice. "The extension and restriction of the trachea, together with its dilatation and attraction, are the cause of the varying of the voice of the animals from high to deep and from deep to high; as to which the second acts and the shortening of this trachea not being sufficient at the rising of the voice, it dilates itself somewhat toward the upper part, which receives no degree of sound and come to raise the voice of this remnant of the shortened pipe. But on this we shall make an experiment in anatomizing the animals, giving air into the lungs and pressing them, narrowing and dilating the 'fistola,' the generator of their voice." There is no specific mention of the vocal cords having to do with the production of voice or sounds. In several of the drawings, the cords are shown and a suggestion of the ventricles of Morgagni. Leonardo implies that these depressions become filled with "omere" and this produces a roughness of the voice. It is possible that some time in the future, the lost treatise on the voice will be found and a better understanding of Leonardo's concepts given to the world.

#### SUMMARY

The documentary evidence established in the reassembled note books in facsimile in the Quaderni D'Anatomia and the Dell' Anatomia, and dealing with the anatomical drawings and descriptions, pronounce Leonardo an anatomist of exceedingly high ability.

He was the first anatomist to make and describe cross and split sections of the human body. He constructed a special fine-cutting saw for this purpose.

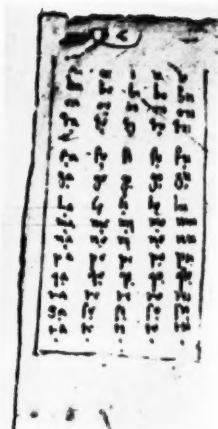
Leonardo's dissections and drawings of all parts of the body, while useful in surface anatomy for a painter or sculptor, are of such scientific value that after 400 years, they are still outstanding.

Leonardo discovered and described the maxillary sinus, also the frontal sinus. He described the facial muscles and their functions.

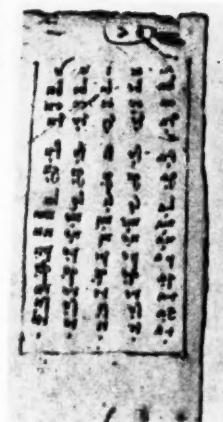
The creator of the Mona Lisa's smile could only be one who understood the action of the orbicularis oris and the risorius muscles. Only an artist-anatomist could produce such a masterpiece, and only because of his knowledge of the pair of muscles "which distend the mouth and prepare it for laughing." (Quaderni D'Anatomia, Vol. 4, Folio 10 Recto.)



A



B



C

V] a r i o v  
 bu be bi bo bu  
 ca ce ci co cu  
 da de di do du  
 e  
 fa fe fi fo fu  
 ga ge gi go gu  
 la le li lo lu  
 ma me mi mo mu  
 na ne nj no nu  
 pa pe pi po pu  
 qa qe qi qo qu  
 ra re ri ro ru  
 sa se si so su  
 ta te ti to tu

Aliter, E: mactata. — R: pueritia, L: u n

D

A. The manuscript deals with movements of tongue and phonetics. In upper right hand corner is seen a table of pronunciation of the vowels. In Paragraph 7 and 9, the principal movements of the tongue are described, while in Paragraph 11 (right lower corner) he states that this discourse does not belong here.

B. Shows a reversal of the writing so that it becomes easily legible to those accustomed to reading characters in words not reversed nor in sequence from right to left.

C. This is an enlargement of the manuscript in the upper right hand corner.

D. Translation. (Quaderni D'Anatomia, Vol. IV, Fol. 10 Recto.)

His anatomical drawings of the larynx, trachea and bronchi are of the earliest recorded. There is no record, at present, of his having described the vocal cords.

His anatomical and physiological explanation of the production of the human voice is, in part, that of today. During Leonardo's time and for several centuries afterwards, there are no records available that discuss the movement of the vocal cords.

His writings and description of phonetics fit very well into our present conception of the production of the vowels and other sounds.

These anatomical studies and writings were vaguely known to exist but it was not until their rediscovery not over sixty years ago and facsimile copies made of them some years later, that they become known generally.

#### COMMENT

Leonardo's contributions to laryngology and rhinology, other than a notation of priority in the anatomical studies in the field mentioned, are merely historical.

As a practical contribution, they are four hundred years late.

Nevertheless, a perusal and study of these anatomical drawings and descriptions must be an inspiration to all of us, because of their accuracy, artistry and beauty.

With all the handicaps of his times against him in the procurement of anatomical material, he succeeded in recording extensive and magnificent studies of human anatomy.

In admiration for Leonardo's constant desire to work to the end, that perfection might be attained, we pay our tribute to this genius and Scientific Magnifico of the Florentine Golden Age.

He said: "The genius of man may make various inventions encompassing with various instruments one and the same end; but it will never discover a more beautiful, a more economical, or a more direct one than nature's, since in her inventions nothing is wanting and nothing is superfluous." (*Quaderni D' Anatomia IV, Folio 10, Recto, paragraph 10.*)

108 E. 38TH ST.

#### REFERENCE

McMurrich, J. Fairplay: Leonardo da Vinci, the Anatomist. Williams and Wilkins, Baltimore, 1930.

SOME DENTAL OBSERVATIONS BY AN  
OTOLARYNGOLOGIST

GORDON BERRY, M.D.

WORCESTER, MASS.

Half a century ago, dental pathology was thought to have an intimate relationship with nasal and paranasal sinus diseases. For instance, Kyle's book<sup>1</sup> on "Diseases of the Nose and Throat" in 1899, refers repeatedly to dental phases. Later investigators felt that this relationship had been over-emphasized. Skillern's book<sup>2</sup> in 1922 says: "Recent years have shown that carious roots of teeth are responsible only for a small percentage of maxillary sinus empyemas, much smaller than was formerly supposed. Statistics now prove that not more than 25% of cases result from this cause while in former years this source would seem to supply from 90 to 100% of all reported cases."

Phillips<sup>3</sup> textbook (in 1928) refers occasionally to dental complications, Coates<sup>4</sup> (in 1929) scarcely mentions them, Imperatori<sup>5</sup> (in 1935) discusses the anatomy of the teeth, and the diagnosis and care of pyorrhea and Ludwig's angina, but makes only brief reference to the effect of dental abscesses on paranasal sinusitis.

With more refined specialization, was there not a tendency on the part of rhinologists to think of the outer margins of the paranasal sinuses as marking the limits of their interest and responsibility? And did we not expect the dentist to consider the floor of the antrum as the ceiling beyond which he had no concern? Such were the accepted procedures in the writer's earlier practice of otolaryngology, when an energetic salesman persuaded him to procure a dental transilluminator. With this he adopted the routine practice of transilluminating not only the sinuses but the teeth in every new office case. A keen dental roentgenologist was willing to review and advise. Through these practical studies and this cooperative effort, the writer gained material help in his diagnostic procedures. Others have made similar studies and have secured similar aid. But the literature is still scanty, and many otolaryngologists still leave the question of a possible contributing dental complication to the patient to discover. This article is presented in the hope of increasing the otolaryngologist's interest in the nearby teeth, and of

bringing him to better appreciate how frequently dental pathology influences the onset and course of ear, nose and throat diseases.

#### MECHANICAL PHASES

##### 1. *Primary Teeth:*

a. *Dentition Sequence.* It will be helpful in this discussion if we have before us the order in which the different teeth appear. The following is quoted from Strang's "Textbook of Orthodontia":

"The time of eruption of the teeth is very variable and the tables given below represent only an attempt to tabulate these data at the average time. As a rule, the lower teeth erupt before the corresponding upper teeth.

##### "The Deciduous Teeth:

Central incisors—fifth to eighth month.  
Lateral incisors—eighth to tenth month.  
First molars—tenth to sixteenth month.  
Canines—sixteenth to twentieth month.  
Second molars—twentieth to thirtieth month.

##### "The Permanent Teeth:

First molars—fifth to seventh year.  
Central incisors—sixth to eighth year.  
Lateral incisors—seventh to ninth year.  
First premolars—Eighth to tenth year.  
Lower canines—ninth to eleventh year.  
Second premolars—tenth to twelfth year.  
Upper canines—eleventh to thirteenth year.  
Second molars—twelfth to fourteenth year.  
Third molars—seventeenth year to any time later."

b. *Tissue Activity during Dentition.* It is a common observation that lymphoid tissue in the pharynx and nasopharynx is more active during dentition. The nasal mucous membrane may share in this congestion. If obstructive pathology results, surgery may be necessary. But the careful surgeon remembers that these hypertrophied tissues tend to atrophy when dentition ceases. By such care



he may avoid corrective surgical procedures which may prove to be unnecessary, and occasionally are of no avail and even harmful.

c. *Early Extractions.* Particularly in out-patient cases, the children may show much dental caries. This caries is usually due to faulty diet, particularly to the ingestion of excessive sweets. If the roots are solid, often the deciduous teeth can be kept to preserve the alveolar alignment for the better erupting of the permanent teeth. But if gumboils or X-ray studies indicate abscessed roots, these should come out, thus securing healthier conditions for the adjacent permanent tooth sacs.

Such childhood extractions may remove a six-year molar. This is a permanent tooth. If removed early, the tipping of the adjacent teeth, with possibly a relative shortening of the bony jaw will nearly obliterate the missing tooth space along the chewing surface in the adult. Excessive tipping can be prevented by orthodontia, if correction is applied early.

## 2. *Palatal Arch:*

a. *Cleft Palate.* Where available, the oral surgeon is the natural man to handle harelip and cleft palate abnormalities. Many communities do not have oroplastic specialists, and these cases will then be handled by the general surgeon or the otolaryngologist. By reason of his knowledge of the anatomy and his constant working in the nose and mouth, the otolaryngologist falls heir to a familiarity and skill in this field, and enjoys a proper claim on this work.

For those who do this surgery a knowledge of the anatomy of the alveolar processes and teeth is important. Three phases may be discussed.

(1) *Anterior Cleft.* In an anterior cleft with an accompanying harelip, the action of the unsupported lip muscles pulls the alveolar processes yet wider apart. An early closure of the harelip reverses this action; now the lip muscles press against the arches, moulding the processes backward and together into proper alignment, and narrowing the cleft at the same time. One school of thought has recommended fracturing or bending the maxillary bones together, or the insertion of approximating wires. But these procedures almost surely injure the unerupted teeth. The writer has tried both methods and has found the gradual moulding by the lips the kinder and more effective procedure. But it must be remembered that the jaws become less plastic as the months go by, and an early closure of the over-riding lip yields the nicest results.

(2) *Posterior Cleft.* The hard and soft palate cleft is best closed by sliding flaps of soft tissue dissected free from the palatal bones. If the cleft is wide and extra tissue is sought, more can be secured if the operation is done before the side teeth have erupted. Then a careful dissection can use the tissue even out beyond the tooth line, and without injury to the tooth sacs; but care must be used. Usually the tissues inside the tooth lines are ample and the operator may wait until the mouth is larger and the tissues tougher. Some wait longer; where he has a choice, the author closes the lip during the first few weeks of life, and the palate before the second year in order to have an intact palate when habits of speech are acquired.

(3) *Orthodontic Aid.* Irregular and crowded teeth are the rule in these cleft palate cases. The final result is better if intelligent treatment is early applied. Faulty eruptions can be swung into line, missing teeth filled in, and a poor bite adjusted, by clever dentistry.

*b. Narrow Palatal Arch, with No Cleft.* The orthodontist formerly waited for the permanent teeth before straightening crooked or crowded teeth. Now he starts as early as at four or five years of age, for the deciduous teeth are much more easily moved than the permanent, and if they can be brought into good alignment, they tend to determine the direction in which the permanent teeth will erupt. A proper amount of gentle pressure makes the young alveolar process grow in the desired direction, while excessive and rapid spreading only loosens and tips outward the teeth, and does not spread or flatten the arch itself. Such broadening if needed and attained, lowers and broadens the floor of the nose and creates more normal nasal passages in adult life.

### 3. *Mechanical Dental Abnormalities:*

*a. Faulty Eruptions and Impactions.* (1) The descent of the permanent molars. In childhood, the alveolar arch is shorter and gives room for five teeth on each side. The adult jaw must lengthen to accommodate eight teeth, and larger ones. Some of these permanent tooth sacs, to find room, lodge up behind the small child's antrum. With growth, the maxillary sinus cavity enlarges posteriorly, the jaw lengthens and the molars swing down into place. In this swinging descent (and in a somewhat similar swinging ascent for the lower jaw) the molars may not erupt vertically. A faulty eruption causes varying degrees of impactions, in which any of the teeth may share though the third molar is the chief offender.

(2) Pain from impactions. When the slanting impacted tooth is due to erupt, the prying pressure from its unsuccessful attempt may cause pathology which first comes to the attention of the rhinologist. Pains referred to the sinuses, ear and head, nasal congestions, recurring colds, and a vasomotor rhinitis with its typical allergic picture: any of these may clear promptly when this dental pressure is relieved. An extreme case in the writer's experience was a typical nasal hay fever condition which cleared when over-straining orthodontic bands were removed, and which reappeared when they were reapplied.

(3) Anterior impactions. The frequency of third molar impactions puts the rhinologist on his guard, but occasionally he forgets to check the bicuspid and incisors and the X-ray picture surprises him with an unerupted front tooth that he supposed had long since been extracted. Supernumerary teeth also may complicate the picture. It is a good rule to count the teeth, especially in a crowded upper jaw, and get a history of extractions for those not showing.

b. *Faulty Bite.* (1) Dental Prying. Two forms of dental prying may be considered. One concerns a leaning tooth where the next supporting tooth has been extracted. Biting on this tooth exerts a leverage that both loosens the tooth and pries on the nerve. This trauma may cause neuralgic pain. The second form concerns an isolated upright tooth (with no nearby supporting teeth) or a high redundant filling, that bears an excess of contact pressure from an opposing tooth. This isolated pressure may cause neuralgic pain either in the offending tooth or in the opposing tooth. Such neuralgic pains may extend up the involved nerve trunk, and if severe may involve others of the trigeminal trunks on the same side.

(2) Over-closure. Of late the literature has emphasized the harmful effect of an over-closure of the jaw, causing an excessive pressing and swinging backward of the jaw condyle in its articular bed. The extreme form occurs when all the teeth are extracted and no artificial dentures take their place. The milder form comes when old dentures do not adequately build up the worn-down bite. The atrophied jaw edges when at rest in the normal position are now farther apart than they were when these temporary dentures were first fitted. In consequence the jaw over-closes, though not as much as when no dentures are worn.

(3) Jaw Leverage. Another cause of excessive pressure in the jaw articulation comes when only the front teeth remain and no dentures are worn. Now the jaw becomes a lever with the fulcrum

at the front teeth. A strong pull with the jaw muscles pulls the condyle up hard against its articular seat.

The pathology from these faulty bite conditions are neuralgias about the ear and radiating out along neighboring nerve paths, and hyperemia and pressure to the ear canal and along the eustachian tube. Cases of conduction deafness have been reported, relieved by the correction of the bite. The writer has observed the clearing of the neuralgic pain and a sense of well-being in the ear as a result of such correction, and also a little acoustic gain in selected cases. But he has not seen the marked gain in hearing that some have reported.

#### INFECTIOUS DENTAL ABNORMALITIES

1. *Superficial Infections.* Pyorrhea and superficial caries are dental problems. But some patients seek aural or nasal aid who do not think it necessary then to consult a dentist. Before recommending more serious surgery, the otolaryngologist will gain material aid in many forms of nasal and oral disease through a clearing up of the mouth infection. Experience shows that in selected cases recurring colds, nasal congestions, occasional attacks of tonsillitis and a periodic otorrhea can improve or clear if strict oral hygiene is maintained. The handicapping effect of dental infections on such conditions as epulis, or mouth or throat cancers, or laryngeal tuberculosis is well known. In seeking such oral hygiene, it will be remembered that the offending organism may be anaerobic.

2. *Deep Infections.* After a superficial caries has entered the tooth and involved the pulp chamber, it passes readily through the root canals to the apices. Such involvement and passage will naturally devitalize a single-rooted tooth. But if there are two or three roots, one root may be dead and abscessed and the other roots remain alive. This introduces the confusion of an abscessed tooth shown to be vital by the dentist's electric pulp tester. A large filling, a hypersensitive tooth, a mild shadow on transillumination and the need of a stronger than normal electric current to get a response, all point to a suspicious condition calling for roentgenological review. This review requires an expert in dental diagnosis who knows how to change the angle of approach and thus isolate and show in the film each individual root under consideration, with its relationship to the jaw and to the antrum. If this review shows a devitalized but not abscessed tooth, the X-ray studies should be repeated yearly, to catch a developing abscess before it can do much harm. Any dead tooth must always be held under suspicion.

3. *Transilluminating Technic.* In his study of dead and abscessed teeth, the otolaryngologist does not infringe on the dentist or roentgenologist. His effort is to employ some quick and reliable technic which will tell him whether to seek the help of these experts. For this he may use a simple dental transilluminator with rheostatic control. His examining room is best artificially lighted and thus easily darkened. With full current on, the lamp is first used to transilluminate the sinuses. If the skull is thin, less current is employed and contrasts are more easily found and evaluated. Then the lamp is dimmed by lessening the current, and the alveolar processes are transilluminated from the buccal, and from the palatal sides. Moving the lamp a little italicizes the shadow.

Pyorrhea and superficial gum infections will show shadows along the gum edges. Deep infections show as shadows more remote from the gums. Occasionally in a multiple-rooted tooth, it can be determined which is the abscessed root. The routine use of the dentalamp will prove most helpful. The writer hopes to find an average of four dead teeth out of five by this quick and easy method, resulting in diagnostic aid to himself and in economy to the patient.

4. *Lower Jaw Infections.* Deep infections in the teeth of the lower jaw concern the rhinologist less. They may be the source of cervical gland swellings, of abscesses in the floor of the mouth or more remote, and of periosteal infections or osteomyelitis. When discovered, a prompt extraction may be indicated, but first one's surgical judgment had best be consulted, for sometimes a precipitate extraction wakes up and extends a process that is trying to wall itself off. Delay here is the part of wisdom.

5. *Upper Jaw Infections.* (a) *Deep Anterior.* Deep anterior dental infections in the upper jaw have a direct effect on the anterior nasal mucous membrane and structures. A septal abscess may have its origin in a dental abscess just beneath; a tendency to epistaxis may be cured by correcting a carious upper incisor; and an anterior turbinal engorgement or even a nasal allergy may show marked improvement when this dental pathology is taken care of. It is not suggested that this must be the sole cause of such nasal trouble, but it may be an essential contributing cause.

(b) *Deep Posterior.* Deep posterior dental infections in the upper jaw are a fruitful source of trouble to the maxillary sinus just above. These infections play so important a part in the rhinologist's work as to deserve detailed consideration.

## DENTAL INFECTIONS IN PARANASAL SINUSITIS

1. *Discussion of Cases:*

a. *Surveys.* Under the title of "Dental Caries in Paranasal Sinus Disease," the writer<sup>7</sup> reported his observations in 152 sinusitis cases before the American Laryngological Association in 1928. Another survey of 73 cases was similarly reported<sup>8</sup> in 1929. His effort was to discover, first, how many patients showed diseased teeth beneath an infected antrum, thus having a "possible" relationship with the sinusitis just above; and, second, in how many cases these discovered carious teeth were apparently proved to be a primary causative factor—proved through a prompt clearing of the sinusitis when the carious teeth were removed.

Listed as "not possible" were those cases in which all the subjacent teeth seemed healthy; as "possible" were those where there was a dead tooth just under the antrum but where no abscess could be demonstrated; as "probable" were those cases in which a dead tooth in the antrum floor did show an abscess, but final proof that it caused the sinusitis had not been obtained; and as "proved" were those where the elimination of a known abscessed tooth in the antrum floor did cure the sinus disease.

1928 SURVEY — 152 CASES OF MAXILLARY SINUSITIS SHOWING  
THE POSSIBILITY OF DENTAL INFECTIOUS ORIGIN.

(Expressed in Percentages)

NOT POSSIBLE	POSSIBLE	PROBABLE	PROVED
11	41	30	18

## 1929 SURVEY — 73 CASES OF MAXILLARY SINUSITIS

(Expressed in Percentages)

	NOT POSSIBLE	POSSIBLE	PROBABLE	PROVED	TOTAL
Acute	5	10	4	1	20
Chronic	3	23	33	21	80
	8	33	37	22	100

b. *Divergent Discussion.* Those discussing these papers felt that either the writer's experience was unique or he had over-emphasized the importance of the dental caries in the probable and possible groups; that even though about 90% of these cases did show nearby dental trouble, this was a coincidence and that in only about one

quarter of our antrum infections did the teeth play a causative part. This divergence was a natural one. The discussors were considering cases where a dental abscess was known to be responsible for the antrum empyema. This figure paralleled the writer's 18% and 22% for "proved" cases. But this survey went farther and tried to discover the less apparent cases, where a "probable" or even a "possible" connection between a dental and a sinus disease could be discovered.

c. *Author's Comment.* In more recent years the percentages are thought not to be running so high, but this can be ascribed to the more intelligent and careful procedures now employed by our dental confreres, with healthier teeth resulting. It is granted that the writer's known interest in this work might bring more to him. But the need for a routine review of the subjacent teeth in all cases of maxillary sinusitis is as important now as it was when these surveys were made, and the carrying out of needed dental extractions will be helpful. The mechanical phases of a blocking deviation of the septum or an enlarged middle turbinate or a hyperplastic membrane or obstructing polypi are borne in mind, but aside from the varying percentages that different men may meet, it may be safely asserted that chronic apical infections in the floor of the antrum are fruitful and frequent sources of sinus and nasal pathology. Such an assertion is built on logic. Antrum empyemas are most frequent in middle life, and it is during this period that dental abscesses are most frequent. Other nose and throat troubles do not appear to be routinely more prevalent during the third, fourth and fifth decades.

## 2. *Progress of the Dental Infection:*

Dental carious processes tend to drain out into the mouth until the offending cavity is filled, after which the only possible drainage, if anywhere, is into the jaw bone or up through the dental canal to just below the antrum. If the antrum is high, a dental abscess forms in the thick alveolar process which becomes demonstrable in the dental film. If the antrum floor is low, the dental infection early breaks through into the antrum cavity without any demonstrable bony absorption or abscess formation in the film. From that time on, all the infection from this diseased tooth bathes the antrum mucous membrane and drains into the nose and back around the eustachian tube. What else should we expect than that this dental infection would slowly but surely create infectious and degenerative changes first in the antrum and later in the neighboring ethmoid cells?

### 3. *Surgical Approach:*

a. *For Abscessed Teeth.* When in training the writer was taught that such degenerative changes in the antrum floor should be approached through the canine fossa. He has since seen so many cases clear by the extraction of an abscessed tooth where on occasion a large alveolar fistula may remain, that his viewpoint has of necessity changed. Now all dead teeth under a diseased antrum automatically come under suspicion. If X-ray studies show them abscessed, the dentist should extract these teeth. If the sinus infection is acute, some delay in the dental extraction is wise. On extraction any necrotic bone around the abscessed tooth should be gently curetted even if this means perforating up into the antrum. It may be inserted here that the dental surgeon who extracts a badly abscessed tooth and so causes a fistula up into the antrum, should not be blamed for faulty technic. Quite the contrary. The blame comes in waiting until the antrum floor is so necrosed that no other result is possible. If the antrum floor is thus perforated and granulations are present immediately about the fistula, these may have to be gently removed. To make a large alveolar opening is grantedly not desirable, for healing is delayed and chewing has to be done on the other side. But the argument that food and infection now pass from the mouth up into the antrum to make this worse and involve the other sinuses, has not proved true with the writer. If occasional food does get up it can be blown or sucked back into the mouth again. Repeated cleansing by irrigation is rarely necessary, and offers the hazard of infecting the ethmoid cells above. The granulating across and ultimate healing usually progress uninterruptedly, with very little help from the surgeon, provided the diseased source has been eliminated and no other abscessed tooth keeps the antrum infection active.

The surgical approach desired then is that which is simplest and most direct, reaching most easily the diseased areas involved. If the antrum disease has advanced so far that these conservative methods are inadequate, then a radical approach through the canine fossa will be necessary. At this stage, an intranasal antrotomy will scarcely suffice. We are not discussing here sinus infections of solely nasal origin. Here the avenues of attack would be through the nose or canine fossa, again, the simplest and most direct approach.

b. *For Non-Abscessed Dead Teeth.* If an abscessed tooth just beneath a diseased antrum should come out, what about a dead tooth where no abscess can be demonstrated in the X-ray film? If the



antrum floor is thick, offering an easily seen bony area where a developing abscess would show, and there is no apparent abscess when looked at from different angles, one naturally employs other measures than dental to cure the antrum. But if the offending dead tooth root reaches up to the antrum floor, offering no room for an abscess to develop and show, and if conservative efforts in the nose fail and the nose does not offer an obvious cause, then the dead tooth is considered a likely source of the antrum infection and is extracted, irrespective of whether an abscess can be demonstrated. Nor need there be dental pain; most abscessed teeth given little or no pain.

#### CONCLUSION

Many otolaryngologists pay relatively little attention to the teeth. With the routine use of the transilluminating dentalamp, the writer has become increasingly aware of the intimate relation between dental pathology and the ear, nose and throat diseases he has been treating. This experience recommends a careful inspection and transillumination of the teeth in every patient. If pathology is suspected, vitality tests and X-ray films should be made by competent consultants. If dental pathology is demonstrated, its intelligent elimination will often clear a trying neuralgia or a recurring nasal trouble or a stubborn sinus infection. The conscientious otolaryngologist who studies the teeth of his patient will find it very worth while.

36 PLEASANT ST.

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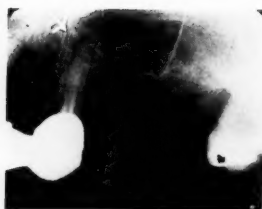


## A. RECURRING HEAD COLDS

Mr. F. E. B., aged 57. Recurring nasal colds. Well-filled apparently negative upper second bicuspid. Extraction relieved colds.

Miss F. S. J., aged 54. Recurring colds, chiefly right-sided, with a mild accompanying right antrum pain. Shrinkage always cleared the process. The upper right second bicuspid was dark on transillumination—a dead tooth but not abscessed and not reaching the antrum floor. Finally the first molar, though transilluminating normally, showed an abscess in the film. This is to be extracted and relief is anticipated. Note how the carious cavity encroached upon the anterior horn of the first molar pulp chamber and so infected the root.

Miss C. K., aged 23. Recurring acute antrum pain with each cold. This abscessed upper left first molar was declared by her dentist to be healthy but was extracted. Antrum cured under local shrinkage, not to recur. Later the partially impacted third molar was removed because of dental neuralgic pains.



## B. ACUTE SUPPURATIVE MAXILLARY SINUSITIS

Mrs. H. E. Q., aged 40. Recurring acute antrum empyema. Teeth and film pronounced all right by able dentist. Upper right second bicuspid dead, reaching antrum floor; no abscess seen. Extraction and nasal shrinkage. Cure.

Mrs. J. E. McK., aged 35. History of rare colds. Antrum infection brought on by abscessed upper right second bicuspid and upper left first molar. Note abscess on side of bicuspid, reaching antrum floor, caused by dental post. These teeth extracted. Cure.

Miss A. S., aged 22. This upper right first bicuspid shows an abscess and a small break through the antrum floor. Extraction. No other treatment. Antrum empyema cleared, also a right-sided tinnitus.

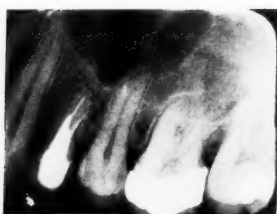


## C. SINUSITIS WITH ALLERGY

Mrs. W. D., aged 35. Recurring hay-fever from grass pollens, with one acute maxillary sinus infection on right. Note the well-filled upper left second bicuspid, with no abscess but a break in the antrum floor. The antrum cleared by irrigation. No recurrence. The hay-fever is mild and therefore the patient has kept this useful tooth thus far.

Mr. P. W. M., aged 47. Nasal allergy for past two years only. These films showed abscessed upper right lateral and first molar teeth and abscessed upper left lateral and first molar roots. The abscessed molars are just beneath the antrum floor. The removal of these teeth without any other treatment cleared the trouble excepting a rare slight sneezing attack.

Miss M. C., aged 26. Animal hair allergy and recurring sinus infections and headaches. Several abscessed teeth were removed with relief. Recurrence one-half year later. X-ray recheck showed covered abscessed molar root remnant. Extraction. Relief, with allergy much improved.

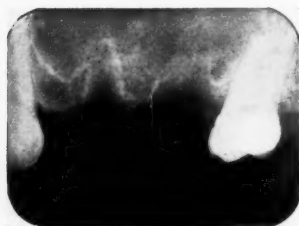
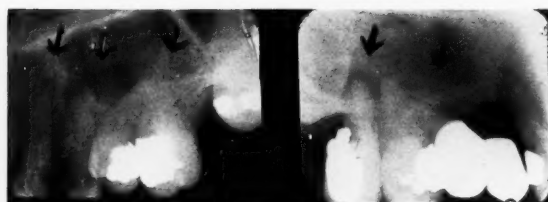




## D. CHRONIC SINUSITIS

Mr. S. B., aged 17 to 30. Severe headaches and recurring bilateral ethmoidal and maxillary sinus infections. Tonsils out, septum straightened, ethmoids exenterated, intranasal antrotomies done. Note the well-filled, apparently negative upper right first bicuspid root canals. Case did not finally clear until the dead teeth were all removed.

Mrs. J. E. C., aged 31. Had recurring right-sided sinus attacks following swimming. Note the clear-cut abscessed upper right second bicuspid which the dentist had repeatedly assured her was healthy. Extraction and a short local use of ephedrine oil cleared the trouble. Later swimming did not bring on another attack.



## E. ALVEOLAR FISTULA INTO THE ANTRUM

Mr. S. C., aged 30. Chronic bilateral maxillary sinusitis. Note the abscessed upper right and left first molars. The septum had been straightened and the tonsils removed by another, without relief. These two teeth were removed causing an alveolar fistula on the left. This antrum was irrigated three times through the fistula and shrinking nasal medication given. No operative work was done. The fistula was healed solid and the sinuses had cleared when he returned three months later for a check-up.

Miss F. C., aged 49. An acute right antrum and an alveolar fistula followed the extraction of the abscessed upper right second molar. Five irrigations through the fistula at spaced intervals cured this side in three months. Two months later the abscessed upper left first molar was removed. Again a fistula and an acute antrum empyema resulted. The granulations in the antral floor were curetted through the fistula and the antrum was irrigated four times. Healing resulted in one month with a closure of the fistula. No recurrence.

Miss M. H., aged 25. Referred by a dentist following extraction of upper bicuspid and first molar with fistula at molar. The antrum was full of foul creamy pus, spilling over into the nose. The fistula granulations were curetted away, and a few irrigations through the fistula nearly cleared the infection. Recurrence. Removal of the doubtful looking second molar seen in film. This proved to be an abscessed tooth. The antrum has cleared and the fistula nearly closed, after four weeks. If this gain is not permanent, a radical antrotomy will be necessary. Note fistula at upper right first molar.

Mr. D. M., aged 39. Referred for infectious focus to explain a left eye keratitis. Is sensitive to green coffee dust and works in coffee store. Left middle turbinate crowds left upper naris; sinuses clear. Upper left first and second molars dark on transillumination. X-ray shows no abscessed roots but a distinct shaded area of granulations or cystic tissue mounding up into the antrum. These teeth carefully extracted by expert. No bony antrum floor found above the first molar but a soft area of granulation tissue immediately above a large alveolar fistula. These granulations were removed by the author, leaving a fistula. The rest of the antrum mucous membrane seemed healthy. The extractions stirred up an antrum empyema. Medication was injected into the antrum through this fistula four times. Fistula healed in two months. Antrum cleared nicely but occasional left ethmoid neuralgias were reported. A left middle turbinectomy was considered, but the condition was not severe enough to warrant the operation.



F. CHRONIC PANSINUSITIS WITH NASAL POLYPI  
AND ASTHMA

Mrs. L. O. McG., aged 43. Had had recurring and increasing trouble over a period of years. An illustrious rhinologist had given her relief by bilateral ethmoidectomies and radical antrotomies. The polyps, sinus pains and asthma had returned. She had been assured the teeth were all right. X-rays showed each upper second bicuspid dead, reaching the antrum floor, with a question of abscess. Extraction of these two teeth cleared the asthma and the pain, and the polyps shrank away and cleared. The only other treatment was nasal shrinkage.

CHOICE OF TREATMENT OF CANCER  
IN OTOLARYNGOLOGY

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EVANSTON

Fifty years ago otolaryngologists concerned themselves little with malignancy. In the volumes covering the first five years of this journal<sup>1</sup> I could find only a few passing references to the subject. The men of that day were interested in the recently perfected technique of the mastoid operation or in their sprays and douches and cauteries. Malignancy was written of in terms of hopelessness. Richardson<sup>2</sup> described an operation of laryngectomy though his patient lived only a few days, stating that "operative interference for malignant disease is sufficiently infrequent to justify one in reporting all cases."

Now nearly every journal in our field contains reports of many successful cases, or describes improved methods of dealing with malignancy. The record has not always seemed cheerful, but in the perspective of these fifty years it is one of amazing promise. If the next fifty years can do as much in this field, it may approach the state of another scientific conquest.

The subject has grown bewilderingly complex. This discussion will attempt some simplification by restating the principles governing the choice of treatment in the light of recent literature and on the basis of 20 years' experience with the head cancer clinic of a large public hospital. This service has been somewhat unusual since its wards were the single repository in a large community for the unfavorable or hopeless lesions in charity patients. The observations made on material so constituted in considerable part, have told perhaps as much the causes of failure as they have the means of cure. They have allowed us at times a check on the accuracy of reports from other institutions, since we have seen patients die in our wards who had been demonstrated elsewhere as cured a few months earlier. These records showed us the fallacies of treatments in earlier days, as for instance the unsuccessful "massacre operations" in advanced cases and the extensive surgical resections before the days of diathermy, the undertreatment by X-ray and radium with later hope-

less recurrence, or of overtreatment with massive doses of poorly filtered irradiation with terrific burns or the more terrible radio necrosis.

In the earlier years the experience was disheartening and it was a register of failure rather than success. Since then the picture has been constantly changing for the better, and the trend is toward earlier diagnoses, less delay in treatment, fewer unwarranted interventions, and a greater willingness not to attempt such cases without proper training or without adequate equipment and proper irradiation. Fewer patients now come who have been exploited or neglected or temporized with.

My own attitude has developed from the time when scalpel surgery was the chief reliance and not even diathermy or roentgen ray or radium was available. The greatest advance has come by sitting before patients with the pathologist and radiotherapist and by study, free discussion and trial, striving to reach a balanced judgment. Probably no clinician or radiologist who lacks such experience or contact and the judicial attitude of mind it brings is quite competent to care for these cases. Certainly the man who is committed completely and in advance to any single method of therapy gives his patients much less than their due chance for recovery.

Certain definite criteria have evolved which seem important in choosing treatment. The choice may be between surgery, usually electrosurgery, or roentgen ray and radium or combinations of these. The criteria may be based chiefly on the clinical course and gross appearance of the tumor, its location and origin, its histologic appearance and probably its histogenesis. Other factors also deserve consideration, including the primary response to irradiation, the patient's general condition, his age and his expectancy aside from the tumor and the possible efficiency of treatment, either surgery or irradiation.

If the campaign first outlined fails, later success is much less likely. If recurrence occurs after irradiation, or if the malignant growth is not checked by it, later surgery will not only usually hold little hope but may even lead to poor healing or serious necrosis. If surgery fails because it is not sufficiently extensive, irradiation will then probably have little chance. Often, of course, combined treatment, as in cancer of the sinuses, may be the treatment of choice, but then should be planned from the outset. A short preoperative course of irradiation may reduce infection and vascularity and inhibit the more fragile and presumably more malignant tumor cells and has been advocated before surgery. It has not often seemed to

me to have been of value and usually has meant only the loss of valuable time. On the other hand, surgery to gain access as in the nose and sinuses and for the removal of the main mass of neoplasm may well be followed by radium or X-ray, which can then do an adequate clean-up job.

Surgery for malignancies in this field except in the larynx should usually be electrosurgery and that chiefly electrocoagulation. Its advantages are relative rapidity and freedom from hemorrhage, shock, and postoperative pain. It seals off blood and lymph spaces against infection and inoculation metastases, and gives smooth healing. Cancer cells coagulated are irrevocably destroyed. It necessarily destroys a zone of sound tissue and may leave mutilating defects, but these can be remedied by plastic surgery or prosthesis. If there is recurrence in the operative wound, it is usually soon apparent and can then be destroyed, although the first operation should be sufficiently radical.

Chemosurgery as described by Mohs<sup>3</sup> has not yet had an extensive trial, but the preliminary report is impressive. As applied to accessible tumors especially on skin surfaces, it permits, after fixation *in situ*, layer by layer excision, and careful microscopic control and mapping of any tumor remaining. This remnant can be similarly treated until all of the cancer is eradicated. Mutilation appears slight and healing good. Excellent training and much patience are required. Of 440 cases so treated by Mohs 93% are well although the post-treatment period is not yet long.

With improving technique irradiation has earned wider use, although there has seemed recently a slight swing away from the high point of enthusiasm for it. Its advantages, properly used, are that it does not terrify the patient, is usually not mutilating, gives better cosmetic results with less risk than operation, attacks a wider field and is usually an ambulatory treatment. Used to the limit of normal tissue tolerance, as it should be used, it will produce real discomfort or even severe pain; over the larynx or pharynx, difficulty in swallowing or even laryngeal obstruction requiring tracheotomy; anemia, cachexia and occasionally the most terrible state of late radium necrosis. Inadequately used it may bury undestroyed cells whose later growth will be resistant to irradiation.

The effect of irradiation is very complex and is not even yet well understood. Many factors besides simple selective necrobiosis of tumor cells are concerned. The stage of mitosis, reactivity of tumor bed, general nutrition and other host factors affect the gen-



eral result. Age, anemia, cachexia, local or general infection and bone and cartilage involvement militate against the best result. Very much has been written on radiosensitivity, and Stewart<sup>1</sup> required 85 pages merely to touch on the high points of the subject.

Each tumor in each particular site must be considered individually in deciding upon treatment, but the criteria above mentioned are likely to be important in the choice. They will be discussed in some detail.

1. *Clinical course and gross appearance.* If a tumor has been of slow growth, if its border is rolled or heaped up suggesting local tissue resistance, if it is papillary or excrescent, if it does not infiltrate and does not fix the tissues in the depth, if it seems somewhat encapsulated, it is likely to be amenable to surgery. If it has grown rapidly, is not papillary or well limited, though it may be fungating, and has not deeply infiltrated, irradiation is more likely to be effective.

If it is of long standing or deeply fissured or ulcerated, if deeply infiltrative, if it has caused much pain, cachexia or loss of weight, neither surgery or irradiation are very hopeful. Regional glands, especially if fixed or matted together, make any treatment much less hopeful.

2. *The location* is important for various reasons which have to do with the parent cell, the tumor bed, its lymphatic and vascular connections and its opportunity to be confined or to invade and its accessibility.

The cancer cell inherits some of the ancestral characteristics of its parent cell. For instance from the flat pavement epithelium of the vocal cord, roughly in 80% of the cases, the tumors are of mature cell type and low malignancy. The same in a degree holds true of the posterior face of the epiglottis and the postcricoid region, of the alveolar ridge and of the skin. On the other hand, from the lymphoid bed of the tonsil and pharynx come largely undifferentiated and anaplastic radiosensitive tumors.

The local lymphatic supply and the vascularity are important, and they may determine the time and extent of metastases. While the frequently mature cell tumor of the alveolar border gives frequent metastases because of abundant lymphatic connections (35% of Ringertz's<sup>2</sup> series) the more anaplastic cell type arising in mid-antrum gives much less tendency to metastases because of poor lymphatics.

The tumor bed is important because not only is its response to irradiation often a potent factor, but it determines often the rate of growth of the tumor and its extension. Bone and cartilage may limit extension very markedly while they may still reduce the effectiveness of irradiation. Tumors growing into the tongue can rapidly extend along its muscle fibres; in the superior nasal chambers they may easily fatally invade the cranium.

Accessibility is a factor of some importance although it frequently has more to do with early diagnosis than with intervention. There is really no area in the realm of the otolaryngologist where cancer can not be reached by the skillful surgeon and attacked when other conditions are favorable. Those in the superior-posterior sinus group, however, above Ohngren's<sup>6</sup> line (from the internal canthus to the angle of the mandible) do not lend themselves so readily to surgery. Similarly the formidable approach to pyriform sinus cancer in relation to the relatively small chance of surgical cure probably should relegate most of these to irradiation.

3. *Histology* of tumors has been stressed as a guide in treatment, but it is subject to strict limitations and some authorities pay little attention to it. Certain principles however should hold, I think, when taken in conjunction with other factors and may well determine final choice. Anaplasia, lack of cell maturity, atypical cells and abundant mitoses indicate in probably 90% of cases of epithelial tumors, sensitivity to irradiation. They usually indicate rapid growth, early extension and early metastases and usually argue to some degree against surgery. Such types in the sinuses and on the cords may, because of other factors, still be surgical, though as New showed in the larynx a greater zone of sound tissue may need to be removed.

The differential pathology of tumors can barely be touched upon in such a discussion as this. Ringertz, in his admirable monograph on tumors of the nose and throat, took 16 closely packed pages merely to list important titles. There is considerable controversy about the classification, grading, and histogenesis of tumors. As to grading there are a good many pitfalls. A biopsy specimen may not be representative of the tumor as a whole, and the histological picture and cell type may vary in different parts of the same tumor. The character of the tumor may change with time, with blood supply, irritation, infection, compression, and other extraneous factors. Metastases may differ considerably from the primary growth. Tumors of apparently identical histologic appearance may run quite different courses. Harris and Klemperer<sup>7</sup> concluded on a

careful analytical study of a relatively small series of carcinoma of the larynx that no histological feature, except possibly frequency of mitoses, gave much indication of the response to irradiation.

Dr. R. Jaffe, who was the very thorough pathologist at Cook County Hospital for many years, disparaged the attempt to grade tumors too precisely but believed that in general the histological appearance was important. Following his lead my clinical experience has seemed to show definitely that tumors with well-matured cell forms, with much stroma, with hornification or other indication of specialization yield well to electrosurgery and often poorly to irradiation. Very immature cell forms, undifferentiated, with little stroma, especially epidermoid tumors approaching Grade IV of Broder's classification, respond very well to radiotherapy.

Certain definite types of tumors have been found, more or less empirically, to have specific response to therapy. For instance the so-called lympho-epithelioma whether of epithelial origin (Schmincke, Ewing,<sup>8</sup> Cutler<sup>9</sup>) or not (Ringertz), melts away rapidly under radiation, usually has metastases when first discovered, which are extensive in proportion to the primary growth and probably never should be treated surgically, but in spite of early favorable response is seldom cured by irradiation. Transitional cell carcinoma grows rapidly and responds well to irradiation, but on the cords and in the sinuses may be limited for some time and be amenable to surgery.

Reticulocytoma (lymphosarcoma, round cell sarcoma, lymphoblastoma) responds well to irradiation at least primarily and usually little can be done for these tumors surgically. Cylindrical cell, or salivary gland type, tumors are affected in most cases only moderately by irradiation though more so than those of the mixed parotid type. True adenocarcinomas and fibrosarcomas including spindle cell types, are hardly affected by irradiation, and are to be cured if at all by electrosurgery.

The histologic architecture of the cells may have something to do with metastases as pointed out by Ringertz who thus explains why cylindrical cells with larger columns less frequently invade lymphatics than squamous cell tumors.

When other determinants fail some authors would judge by the initial response to irradiation whether it is likely to succeed. Coutard<sup>10</sup> stated that if two weeks of fairly intensive treatment showed little effect, surgery, which would still be possible, probably should

be tried. That decision however could usually be made at the outset unless one is primarily committed to irradiation.

The patient's condition should, as Jackson<sup>11</sup> pointed out, help determine treatment. Surely no radical treatment should be used which will not increase an expectancy which is already limited by some other disease, or at least make remaining years more livable. For that reason advanced tuberculosis, diabetes, cardiovascular or renal disease weigh heavily for irradiation in cancer of the larynx. I have not found well-treated diabetes as a rule elsewhere to bar electrosurgery.

From the foregoing it should, I think, be obvious that biopsy is essential to proper treatment, as most authorities agree. Especially must Salinger's<sup>12</sup> comment be emphasized that statistical reports have to be thrown out of court unless based on microscopic evidence of malignancy. Biopsy in doubtful lesions is also most valuable in making an early diagnosis, which is still the most important factor in cure. If positive, it must be followed immediately by treatment.

Otolaryngology should contribute to early diagnosis considerably more effectively than it has, by reason of the accessibility of the field to examination if all methods are used, including direct illumination, mirror examination, the nasopharyngoscope, endoscopy, and roentgen ray including laminagraphy, to discover lesions and to localize and delimit them, which is important in the choice of treatment.

The foregoing statements have had to be rather categorical because of the limits of space. Considerable latitude must be allowed them especially to the skillful, courageous and experienced operator and perhaps also to the studious and courageous and meticulous radiotherapist.

Even more controversy has developed in the consideration of specific regions, but it seems to this writer that there is a considerable agreement among clinicians who have followed a good many cases. In such a wide field one can hardly enter into any full discussions or cite many of the excellent statistical studies or give credit for the outstanding work of many of our colleagues. An attempt will be made, however, to outline briefly treatment in the various regions.

Skin lesions of most types may be treated by either surgery or irradiation, though I have believed, as New recently stated, that electrosurgery is definitely safer, though the cosmetic advantage may

be with irradiation. Basal cell carcinoma, if early, should be cured by either. Squamous cell carcinoma even if of very mature cell type can usually be destroyed by an epidermicidal dose of radium or roentgen ray. Around the eye the cosmetic effect makes the preference for radium although the question of lens injury must be considered even with best efforts at screening.

In lip cancer, local radon implantation, pack, or wedge resection give excellent cosmetic results. The best results in the more extensive lesions have apparently been given by electrosurgery followed by local radium and regional X-ray. Carcinoma of the buccal mucosa is in about the same category. The overlying skin can at times be saved by reflection before coagulation.

Carcinoma of the tongue is an unfavorable lesion since it is usually of an infiltrating type, invades early along the muscle fibres and into the free abundant regional lymphatics and occurs typically in foul mouths with infection (about 40% of our cases had a luetic history). Most of these we now treat with radon implants and regional X-ray or radium. If the lesion involves the tip or border of the anterior one-third of the tongue, if it is papillary or fungating without fixation, electrocoagulation gives a high percentage of satisfactory results. If the floor of the mouth is involved especially with invasion of the bone or fixation over it, I think electrocoagulation is usually necessary. The posterior two-thirds of the tongue is more often involved by an infiltrating lesion and the outlook is bad, and probably local radon and external irradiation should be used. If the lesion has arisen from the epiglottis or the epithelium of the pillars and as yet lies superficially, coagulation may be useful.

Cancer arising from the oral mucosa around the maxilla quickly involves bone, metastasizes relatively early on account of the free lymphatic drainage and yet is fairly favorable and responds less well to irradiation than electrocoagulation.

For malignancy involving the sinuses and nasal chambers, combined treatment seems the treatment of choice following the methods of New<sup>13</sup> and Ohngren with about 38% recoveries. Electrocoagulation is used to gain access to very radiosensitive tumors or to destroy as completely as possible more resistant forms, followed by radium locally and X-ray over the regional glands. Ringertz<sup>12</sup> studies of his own material and cases from the literature have given much help on tumors here and in the nose. Those of the lower third of this area which arise primarily outside the sinus most often yield well to surgery though metastases are common. At or just above this level

in the sinus or nasal chambers the tumors are less favorable and combined treatment gives best results. Least favorable are those in the upper one-third of the nasal sinuses and nose where more reliance must be made on irradiation.

Good exposure can be secured by sublabial approach, or by an oblique lateral rhinotomy incision extended if necessary over the antrum, which gives good exposure yet heals with relatively little scar. Higher up a Jansen type external sinus approach gives good access. I was able through an inverted U incision at the root of the nose, to coagulate successfully an adenocarcinoma which filled the nose and all nasal sinuses except the sphenoids and extended well into the nasopharynx. The patient is well after eight years.

I have only one cure of carcinoma of the tonsil by electrosurgery, and this probably arose from the posterior pillar, although in earlier days I made many attempts. Coutard, Duffy and others have reported from 28 to 20% of five-year cures in this area, and I now believe coagulation should not be used here except perhaps after the technique of Berven<sup>11</sup> to destroy a small residue of cancer after intensive irradiation.

Carcinoma of the epiglottis is likely to be of the mature cell type and usually will erode the cartilage and eventually spread to the base of the tongue. It is less likely to respond to irradiation. The best technique for its removal seems that of removal under suspension by electrosurgery (Lynch, New) which also permits destruction of extension to the vallecula or epiglottic folds. The removal by thyrotomy as described by Tucker, is satisfactory if the growth is localized or spread down the anterior laryngeal wall.

The other tumors of the pharynx are likely to be anaplastic, spread early and widely by lymphatics, respond primarily well to irradiation, but tend to recur in the glands. Few are cured, as Furstenberg<sup>15</sup> has emphasized, but they should be given the opportunity of treatment by irradiation. Pharyngeal carcinoma can be whipped up by surgery and even by electrocoagulation, which should almost never be used.

Occasionally a postcricoid growth is of low enough virulence and is diagnosed early enough that it can be removed surgically. There are however very few operators who have the temperament and skill to justify the radical external approach which gives relatively few favorable reports. With the exception of tumors of the epiglottis and a very few others well delimited and of mature cell type,

accessible to diathermy, there seems little indication to treat any cancer of the pharynx except by irradiation.

For carcinoma of the larynx, Jackson and Hautant<sup>11</sup> have outlined sound principles. Nowhere does surgery give more brilliant results than in well-localized cordal cancer in cases without fixation and not involving the posterior one-third, with cures up to 88%. Even if the anterior commissure is involved the Jackson technique offers, with its 70% of cures, a result that justifies the small extra hazard. Nothing in my experience indicates that primary treatment of such cases should be by irradiation, and I think it extremely important that the general physician and the public should know this, although some radiologists have used their better opportunity for propaganda to create a strong opposite impression. In the case on the borderline of operability by thyrotomy, histology may make the decision, and the 20% of relatively undifferentiated cancers probably should in doubtful cases have the benefit of more radical surgical procedures or irradiation.

For cordal malignancy extensive enough to indicate laryngectomy, irradiation may be an even choice. The radiologists seem, however, to have lost some of the earlier enthusiasm, and they, like the surgeon, consider cases with infiltration and fixation less favorable. Coutard's earlier report of 27% of five-year cures of cancer of the larynx by roentgen ray has had to be modified by his later report that one-third of those later developed recurrences, and this hardly compares with the well over 50% of definite cures for surgery.

Subglottic tumor is usually infiltrating, radio-resistant, more extensive than thought before operation and there seems little question that it requires laryngectomy, or perhaps if unilateral, hemilaryngectomy after the technique of Hautant.

Tumors of the ventricular bands have usually extended posteriorly but also respond well to irradiation, which here is probably preferable. Those above this area also have usually extended too far for any but the most heroic surgery, and irradiation probably should be used on them. The relatively rare cancers of the sinuses of Morgagni are usually radioresistant and require laryngectomy if operable at all.

Cancer of the auricle is frequently a deceptively innocent lesion which has advanced much farther along the perichondrium than suspected. Although I have numerous individuals grotesquely ear-

marked by my successful surgery, except in very early cases in most instances I should advise complete removal of the auricle and coagulation into the canal. It does not seem to me that irradiation has done much for these patients.

Middle ear and mastoid carcinomas are usually mature, invasive and are not diagnosed until bone is involved. Removal by bone instruments with clean-up by electrocoagulation offers some possibility of cure.

Carcinoma of the esophagus is at about the stage of surgery where cancer of the larynx was 50 years ago. Some of the obstacles, notably infection and pulmonary collapse and hemorrhage, that have been considered inherently forbidding seem to have been surmounted, and enough cases have been successful by surgery to make a real promise for the future.<sup>17</sup>

Cancer of the lung belongs to the chest surgeon or possibly the radiologist, but there are numerous reports of the successful destruction of malignancy of the trachea by diathermy.

In spite of progress the cures of important lesions of cancer are still a minor fraction of the total. Yet with optimism and early diagnosis, by making use of present methods guided by even our present meager knowledge, there is much hope for the sufferer of malignancy. Even if the longed-for revolutionary method of complete destruction of all cancer cells does not materialize, advances for another 50 years at the present rate should make cancer one of the minor episodes instead of the nightmare it has been.

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ABSORPTION OF QUININE INTO THE CEREBROSPINAL  
FLUID OF THE FETUS IN UTERO

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Quinine as an etiologic factor in the production of deafness in newborn infants is now an accepted entity. Much work has tended to establish for quinine and its therapeutically employed salts the status of a protoplasmic poison. This pharmacologic characteristic exerts its influence directly upon the sense organs, especially in the case of the external hair cells of the organ of Corti. Thus this drug may imperil the delicate aural mechanism not only of adults and children but of the fetus in utero as well, through its presence in the maternal circulation.

In our approach to the subject it has been argued that by reason of the deleterious action of quinine, in some cases, on the ganglion cells of the cochlea and the endothelium of the small blood vessels of the internal ear, and because of its tendency to diminish the pressure in the endolymph, there occurs a series of events culminating in ischemia, anoxemia, lack of nutrition and eventual degeneration of the ganglion cells and the nerve fibers in the basal coil of the cochlea. All of these conditions have been demonstrated, together with similar effects caused by certain other drugs, by competent investigators, whose works are recorded in the medical literature of the past two decades.

Upon the thesis that quinine is capable of causing harmful changes in the delicate cytology and finely adjusted mechanism of hearing in the newborn, we first assumed that to be responsible for such effects the drug must be present in the nourishing or trophic humors of the auditory apparatus itself; that the presence of quinine should be demonstrable, unless its concentration be extremely low;

and that its presence in the cerebrospinal fluid of the newborn infant is *a priori* evidence of its contact with the finer structures of the organ of hearing. This phase of the subject presents a fruitful field for continued research. As Taylor previously stated, the presence of quinine in the cerebrospinal fluid suggests an important analogy between the stria vascularis, which elaborates the endolymph, and the choroid plexus, which is responsible for the secretion of the cerebrospinal fluid. In such a manner the hair cells of the organ of Corti may be bathed in endolymph containing quinine.

In our first attempts to bring evidence to bear upon the relationship between the administration of quinine and deafness, two of us showed that this alkaloid was present in the cerebrospinal fluid of women in whom labor had been induced by this means. Other investigators revealed that quinine can be detected in other body fluids and excreta. It was then decided that the establishment of the presence of the drug in the cerebrospinal fluid of an infant delivered of a mother treated with quinine would give strong evidence of the implication of the substance in the causation of nerve deafness acquired in utero.

Finally, the basis for this reasoning is threefold: (1) the known permeability of the fetal-maternal membranes for crystalloid substances, (2) the finding by various investigators of quinine and other drugs in the blood serum and excreta of animals following their administration to parturient mothers, and (3) the unmistakable evidence, both clinical and histologic, of damage to the internal ear of such fetuses. Then, too, the symptoms of the effect of quinine in susceptible persons may be cited as evidence that upon its absorption into the fetal circulation, the extremely delicate auditory apparatus may give similar response.

For the work undertaken at this time with prenatal cases the mothers were selected for their general normal tolerance of quinine. The obstetric and pediatric services of the Duval County Hospital, Jacksonville, Florida, consented to cooperate in this undertaking in order to control the administration of the drug and to perform the subsequent lumbar punctures. Patients were chosen preferably from primiparae because of the obvious difficulty in obtaining sufficient concentration of the quinine in the short time usually experienced in deliveries of multiparae, especially with the added effects of quinine.

At first indication of the onset of labor the subjects were given daily doses of quinine bisulphate orally in amounts of 5 gr. of the

salt three or four times a day. One patient received a total of 120 gr., but the amounts varied from that to 30 gr. In fact, after the first five cases had been treated, it was found that even low intakes of 30 gr. were sufficient to produce positive results in the fetal cerebrospinal fluid and urine. These figures are not out of proportion with the doses obtained in the attempt to induce labor routinely. Castor oil was, of course, not administered because the desired effect was not primarily to precipitate delivery, or even labor.

Our observations are based on the examination of seven cases in which the mothers were thus treated previous to active labor and delivery. The results obtained substantiate the correctness of our theory of the presence in the fetal cerebrospinal fluid of quinine derived from the maternal circulation, and they likewise corroborate the reports of investigators regarding its presence in the urine. The work entailed was beset with many unforeseen difficulties that so often perplex investigators. The final successful demonstrations were accomplished only recently, although evidence of the presence of the drug in the specimens first analyzed was substantially, but not conclusively, obtained.

#### CLINICAL PROCEDURES

Forty-eight hours after birth, each of the seven infants was carefully subjected to lumbar puncture. From 7 to 10 cc. of cerebrospinal fluid was obtained, and this fluid was then tested for the presence of quinine. Only one withdrawal from each child was made. In the last two of the seven cases, specimens of urine were obtained and tested for quinine. At this time no attempts were made to further the demonstration of the drug in the mothers.

#### CHEMICAL PROCEDURES

Considerable time was spent in the determination of a sure means of detecting quinine in the specimens. A microchemical method was finally worked out which, after many trials, proved sufficient to detect the alkaloid in normal cerebrospinal fluid experimentally inoculated. By dissolving known quantities of quinine bisulphate in normal fluid obtained in routine laboratory procedure, tests were made to determine the sensitivity of crystallizing agents as well as of the several color reactions in serial dilutions covering a wide range. At first this was considered a necessary expedient because of the small amounts anticipated in the actual test specimens. Later refinements in the method evolved showed, however, that con-

centrations attained are adequate for demonstration of crystalline precipitates, at least in the specimens of urine, and for obtaining color reactions in the extracts of cerebrospinal fluid. We were definitely successful in procuring photographable crystalline precipitates in only two of the specimens of urine, and positive color reactions in two specimens of the cerebrospinal fluid; but these were in cases receiving a minimum intake of quinine. It is anticipated that from now on, with the present more adequate procedures, examination of specimens of cerebrospinal fluid containing higher concentrations of the drug will disclose incontrovertible evidence of the characteristic crystal patterns.

In the earlier attempts to isolate the alkaloid in the specimens of cerebrospinal fluid, the method was briefly as follows: For each cubic centimeter of the specimen 0.25 gm. of ammonium sulphate was added, and the solution was brought to a pH of 8 to 9 with ammonium hydroxide. This solution was twice extracted with ethyl acetate, and several extractions with a mixture of chloroform and ether followed. The solvent was then evaporated and the residue taken up with a small amount of chloroform, which was made alkaline and placed in a microseparatory funnel. It was then centrifuged and separated, and the aqueous layer was discarded. This process was repeated, and then the solution of chloroform was acidified, thereby removing the alkaloids that are acid-soluble but alkali-insoluble. The acid solution was next extracted with ethyl acetate and the mixture of chloroform and ether; the solvent was discarded. The acid solution was alkalinized and shaken with ethyl acetate, and the solvent layer, containing the residue of quinine, was evaporated.

It was early evident that a troublesome gel formation resulted as soon as the first extracting substances were added to the alkaline solution of ammonium sulphate. The gel continued to persist and offered a perplexing difficulty since in it the quinine is dispersed in small amounts in a buffered protein medium that defies all efforts to break it up permanently. Until the recent modification, which suppressed formation of this gel, the procedure was to break it up mechanically, extract it while thus dispersed and repeat the procedure indefinitely in the hope that multiple extractions would subsequently contain enough of the residue to answer to final tests.

At this point it was noted with interest that in some of the experimental fluids from syphilitic patients there was, in the final evaporations, an oily residue that defied crystallization and further evaporation. This condition was not observed in the fetal fluids nor

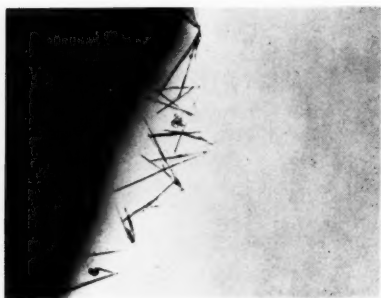


Fig. 1. Photomicrograph showing quinine crystal pattern formed with 2% potassium chromate solution. (X75)

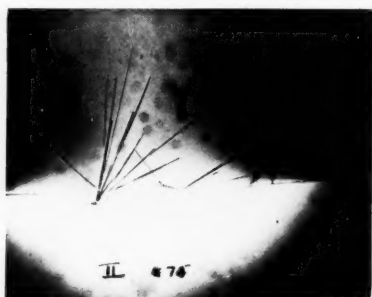


Fig. 2, Case 6. Photomicrograph showing quinine crystals recovered from fetal urine with 2% potassium chromate. (X75)



Fig. 3, Case 6. Photomicrograph showing quinine crystals recovered from fetal urine with 2% potassium chromate. (X330)

in fluids from nonsyphilitic subjects. Its significance offers another problem which we are investigating.

The results obtained by this procedure were not conclusive of the presence of quinine. The evidently low concentration of the alkaloid in the residue was insufficient to produce conclusive color tests, although these tests were slightly positive in a few instances. Furthermore, there was no hope of getting crystal patterns such as were obtained in the experimental control fluids. It was established, however, that the quinine present in the fetal cerebrospinal fluid was in a higher order of dilution and that the need was evident for a refinement of sensitivity tests adequate for detection by means of crystallization rather than by color reactions. Thus it was also evident that concentrations of a minute order are adequate for the production of pathologic changes in the fetal ear.

Upon obtaining the final residue as described, the quinine was crystallized. The characteristic crystal pattern shown in Fig. 1 was procured by using a 2% solution of potassium chromate as a crystallizing agent. This process is one requiring considerable attention, due to the tendency for the formation of potassium chromate salts, which mask the desired pattern, especially in the effort to get photomicrographs. The structures here reproduced were formed from extractions of normal cerebrospinal fluids treated with quinine in a dilution of 1:10,000, which by this method marks the upper limit of sensitivity in these tests.

By combining the extracts of specimens from three subjects it was possible by using a modified thalleoquin procedure to get definite, but not completely conclusive, color reactions for the positive presence of quinine in these fluids. This procedure indicated a possible order of concentration in the original specimens of 1:2,000,000. The color reactions, which, according to our preliminary observations, are overrated as to sensitivity by their proponents, were obtained in probable dilutions of 1:25,000, still too great for the present method of conclusive isolation. In terms of quinine alkaloid, the amount dealt with under these circumstances was substantially smaller, considering the differences in the amount of the bisulphate salt administered. That is to say, the greater molecular weight of bisulphate produced correspondingly smaller quantities of extractable quinine alkaloid.

More recently we devised the following procedure by means of which we successfully produced crystal patterns capable of being photographed.

*Urine.* To 20 cc. of urine was added 5 gm. of ammonium sulphate crystals and ammonium hydroxide to a pH of 8 to 9. The sample was divided into four equal parts and, with ether added to each part, was shaken for from five to ten minutes in a graduated centrifuge tube. The tubes were then centrifuged and the ether layers withdrawn and evaporated on the steam bath. Four such extractions were made and the extracts combined. The ether layer was green in color, and upon evaporation there remained a stringy green mass. The residue was then taken up with 1/10 N. acetic acid, shaken and filtered, and the residue discarded. The filtrate, clear and practically colorless, was made alkaline with ammonium hydroxide and extracted four times with ether. The ether extracts were evaporated and the residue taken up with a few drops of 1/100 N. acetic acid. Distilled water was added to make a total volume of 5 cc., and this solution was divided into two equal parts. One 2.5 cc. portion responded positively to a modification of Abenson's erythroquinine test. The other portion was made alkaline with ammonium hydroxide and extracted four times with ether, which was then evaporated, and the resulting residue was taken up with 0.5 cc. of dilute sulphuric acid. Three drops of this acid solution, when treated with one drop of a 2% solution of potassium chromate, gave characteristic crystal patterns showing the presence of quinine. Figures 2 and 3, in magnifications of 75x and 330x, show the crystals.

*Cerebrospinal Fluid.* To 8 cc. of cerebrospinal fluid from one infant 2 gm. of ammonium sulphate was added, and the solution was made alkaline with ammonium hydroxide. It was then extracted four times with ether, and the extracts were evaporated. The residue was taken up with a few drops of 1/100 N. acetic acid, and distilled water was added to bring the volume to 1 cc. Abenson's erythroquinine test was positive on this preparation.

By comparison with solution of known strength, the concentration of quinine in the sample appeared to be from 1:250,000 to 1:300,000. Since the test solution was eight times as concentrated as the cerebrospinal fluid, the approximate concentration of quinine in the cerebrospinal fluid was 1:2,000,000.

The decision to use ether as the solvent was made after the obstacle of the troublesome gel formation was found to be insurmountable. Although it is inferior to chloroform, there results finally a sufficient concentration to produce crystals in the urine and a positive color test in the cerebrospinal fluid. In the longer method there was obviously a serious loss of material.



## CONCLUSIONS AND SUMMARY

The harmful effects of certain drugs on the auditory mechanism are no better characterized than in the case of quinine. Because of the wide use of this alkaloid in the treatment of diseases concurrent with pregnancy and in the induction of labor, an investigation of its presence in the circulating cerebrospinal fluid was undertaken.

Quinine was detected in the cerebrospinal fluid and the urine of seven infants delivered of mothers receiving oxytocic doses of quinine bisulphate, and it is anticipated that higher concentrations of the drug will produce similar conclusive results with regularity. Although the findings presented do not represent a large number of cases, it is felt that a beginning has been made and that an important piece of evidence has been discovered to the effect that quinine should be used with caution in diseases concurrent with pregnancy, and that its indiscriminate use as an oxytocic drug may have malignant influences upon the fetal ear.

We desire to express appreciation for the facilities placed at our disposal through the kindness of the Florida State Board of Control, President John J. Tigert and Dean Townes R. Leigh of the University of Florida, and the Duval County Hospital of Jacksonville.

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CONTINUATION EDUCATION: A RESPONSIBILITY  
OF OTOLARYNGOLOGY

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WATERVILLE, MAINE

No branch of medicine has been more active in efforts for improvement of its specialty than has otolaryngology. Its Board of Certification, in its 16 years' existence, has proven of inestimable value in raising the standards of practice in the specialty. Its leaders have concerned themselves with the problem of providing adequate preparation in the basic fundamentals and with the curricula of post-graduate residencies. The programs of its several scientific societies and of its well-conducted special periodicals, offer abundant opportunities for keeping thoroughly up to date. Admirable as this all is, it fails to take cognizance of the one most serious defect in our system of medical education. This defect is that the physician often lacks either the initiative or the facilities or both for making use of these opportunities.

Without doubt our medical schools are providing the finest possible medical education in the world today. One weakness in the present system, however, is that everything is concentrated upon the four medical school years and little or no attention is paid to the 30 or 40 tremendously important after-years, when the physician is in active practice in a constantly changing, advancing profession. This would not be a pertinent criticism if the graduates of our schools, in this subsequent period of active practice, were universally imbued with the scientific urge to keep abreast of the latest developments, or were under constant stimulus or pressure to do so. As it is, there is nothing to prevent a physician from practicing his profession with the same limited mental equipment he possessed upon graduation from medical school. Unfortunately there are too many physicians who fail to keep abreast and who become quite incapable of rendering adequate modern medical service to the public. It is this defect that our present system of medical educations fails to correct and which can be compensated for only by some program of graduate or continuation education.

## THE NEED FOR CONTINUATION EDUCATION

To a large extent, our leaders in medicine are teachers and, as such, have had a majority of their contacts with students, both undergraduate and postgraduate, or with physicians practicing in the more nearly ideal conditions of the teaching centers. They have not been intimately associated with the physicians remote from these centers, after the latter have lost the momentum resulting from the medical school and the teaching hospital.

While the observations contained in this paper are necessarily limited in scope, they at least represent a different viewpoint from that of the teacher in the medical school or the physician engaged in postgraduate instruction. They are based upon a number of years' work on graduate education in a state without a medical school or large teaching centers. In many instances, it has meant dealing with physicians whose mental assets are frozen. While this work has been concerned with the profession as a whole rather than with any one specialty, it has necessarily included the specialties, and therefore certain observations and deductions are quite pertinent to otolaryngology.

Good medicine means modern medicine, utilizing every scientific advance which may be of benefit in the treatment of disease conditions or which may serve to alleviate human suffering. It means making intelligent use of every new development which may safeguard the patient or which may eliminate the hazard of loss of function or of life. This demands constant study on the part of the physician, in other words a program of continuation education. The conscientious, progressive physician tends to pursue such a program independently and on his own initiative. This implies the consistent reading of contemporary medical literature, attendance at national and sectional meetings of scientific societies, visiting other clinics and teaching centers, and active participation in hospital staff meetings in which the work of the physician and his confreres is carefully analyzed and evaluated. Unfortunately all men do not have either the desire or the opportunity to follow such a course. Too many are satisfied to continue to practice with the limited mental equipment they possessed upon graduation. Many are carried along for about five years by the mental momentum of medical school or hospital, and then fall into a rut, a rut which is constantly deepened by increasing ignorance with its accompanying smugness and complacency. They start out to practice fairly modern scientific medicine, but soon lapse into a state of mental sluggishness. There is too often an inertia, a willingness to do without necessary

facilities, which a little effort would make available. There is a willingness to accept lowered standards as necessary and a disinclination even to attempt improvement. The necessity of making a living and the vicissitudes of practice may seem an almost insurmountable barrier to progress. And many times the physician is so situated, geographically or economically, that it is really difficult for him to keep abreast in his profession and too easy to sink into a rut. He may lack the stimulus, the contacts, of an environment conducive to progress. Few can work scientifically alone. Yet the same person might be spurred to a continued mental activity by a proper stimulating environment.

Perhaps the greatest curse of medicine is provincialism. This is true whether it be urban or rural, but its results may be more apparent with the latter. There is the danger of the limited viewpoint, basing conclusions on inconclusive evidence. The isolated individual, isolated geographically or mentally, bases his conclusions on his own limited experiences, without careful evaluation, and knows or cares little about the scientific developments, the carefully deduced conclusions, of the profession as a whole. The importance of a program of continued education to combat and correct this situation is becoming generally realized. How to make this most effective and far-reaching is the problem facing medicine today.

#### THE GENERAL PROGRAM IN MAINE

Conditions may vary in different sections of the country, and no one program so far developed seems applicable everywhere. In Maine we have been able to make progress, largely through certain fellowships provided by the Bingham Associates and the Commonwealth Fund. These enable us to send a number of our physicians each year to some teaching center, usually Boston, for intensive post-graduate courses. They carry a stipend sufficient for all living expenses. As far as possible these fellowships are assigned where there seems to be the greatest need for them, with the objective of improving standards of practice in the community. We frankly admit that these courses are a form of "spoon-feeding" and as such cannot begin to compare with that most valuable form of education, self-education, carried on by individual initiative because of the constant urge to practice only the best medicine. But they are excellent as incentives and seem to be the best solution of the problem as it concerns the general practitioner, especially in the smaller localities. In addition we have endeavored to make both the annual meeting of the State Medical Association and its fall clinical session predominantly

teaching in character. We are cooperating in the New England Postgraduate Assembly, a new venture but one whose value has already been proven. We are now striving to develop teaching programs in the hospitals throughout the state.

#### RESULTS OF SURVEYS

As a result of surveys and of a comprehensive questionnaire sent to every member of the State Medical Association, we have estimated that about 10% of our physicians are independently carrying on their own program of continuation education, somewhat in the manner just outlined. Approximately 15% have received the benefits of these postgraduate fellowships referred to above. Of the remaining 75%, one-third are too far advanced in years to expect much of, and another third are indifferent, seemingly quite beyond being awakened from their lethargic state by any means at our command. The remaining 25% have possibilities, show an interest in attending clinics, but as yet have not been brought into our present program. I rather imagine that this situation is not peculiar to us but is typical of the country as a whole.

In our questionnaire we asked the reason for not taking postgraduate courses and attending teaching clinics or meetings of scientific societies. Some of the replies to this question are a bit illuminating, and might be applicable to the situation in otolaryngology. The following are samples: "Too busy," "Lack of time," "Practice too large to leave," "Unable to leave business," "No need for it." This is a cockey one, "As a country doctor I feel that I know more than many of the so-called big clinicians who would teach us. Give me the facilities and I will rewrite Osler." And finally one which illustrates one of the greatest evils in the practice of medicine, "Some of my good patients have been lost to other doctors when I was away and they keep them, also get the appendix out of some." Change appendix to tonsils and, I fear, the statement applies to otolaryngology.

#### APPLICATION TO OTOLARYNGOLOGY

It may be asked how all this affects otolaryngology. We must admit that the average men practicing otolaryngology differ but little from those in other fields of medicine. We have our backsliders, our men in a rut, indifferent, lacking in the most modern scientific outlook, and cursed with the same smugness and complacency, just as have the others. They may be less in proportion to some other fields, but they exist nevertheless.

Our figures for otolaryngology, while necessarily limited in number, are, I feel, even more accurate than those of the general survey, as they are based on a more personal knowledge of the situation. It can be assumed from our survey that one-third of those actively engaged in practicing otolaryngology are satisfactorily carrying on a program of continuation education. Excluding the young men, in the specialty five years or under, and considering only those not possibly coasting under a mental momentum, we find this reduced to about 25%. Perhaps the most disturbing observation is that of the younger men, in the specialty five years or under, fully 50% are apparently making no effort for improvement. This indifference may be traced, in the main, to inadequate training and to lack of proper perspective. It is in this group that there is need for some attention, as these young men will be the active practitioners of the future. Of the older men who are indifferent to any sort of program of continuation education, about 25% have had adequate training and opportunities for keeping up to date. So this shows that while proper training in the specialty is a big factor, it is not the only one; and while efforts to improve conditions at the source, i.e., the medical school and teaching hospital, will accomplish a good deal, they will not entirely remedy the situation and that some program of continuation education is highly desirable in otolaryngology.

#### SUGGESTED PROGRAM

What sort of program would be most practical and effective for otolaryngology? The situation is quite different from that of general medicine. Short postgraduate courses, provided on a fellowship basis, may be necessary in the case of the rural practitioner but are hardly desirable for the specialist. He should be willing and able to carry on his own program. It is largely a question of providing the necessary stimulus. The work of the American Board of Otolaryngology in certifying men upon examination has proven to be the greatest factor in the improvement of our specialty. With the constantly increasing number of hospitals requiring certification in order to qualify for major staff appointments, the influence of the Board has become widespread. This can and should be augmented by the individual efforts of the older otolaryngologists, who should encourage the younger men to seek certification. But this is not enough. One of the fallacies of medicine is the assumption that once a man has been graduated or certified, he is, and will be for all time, competent and safe. While the desire for certification is a most effective stimulus for improvement, the process should not stop there.

In most cases certification naturally leads to membership in the American Academy of Ophthalmology and Otolaryngology. This organization offers what is probably the best teaching program of any medical society. Short but intensive, it should be considered on the "must" list of every young otolaryngologist. As stated before, the meetings of our other special societies and our several excellent periodicals offer abundant opportunities for keeping abreast of the latest developments.

*The Place of the Hospital in Such a Program.* We have suggested that the ideal program will not be a sporadic series of postgraduate courses but a continuous, constantly participated-in program of self-education, whether for general medicine or otolaryngology. For this to become truly effective in any large way it must be decentralized so as to reach the greatest number. Our studies indicate that the hospital is the most fertile field for this program. Seventy-three per cent of those answering our questionnaire indicated that they regularly attended some hospital staff meeting. We do not refer merely to the so-called teaching hospital. The community hospital must assume the responsibility for this program and become, in effect, a teaching hospital. Size or the number of patients need not be a deterring factor. There is plenty of teaching material in any hospital, if it is only recognized and made use of. All that is needed to make a teaching hospital is one patient and some inquiring minds on the staff of physicians attending that patient. The far-reaching effect of the hospital upon clinical practice is not generally realized. Almost every improvement in standards of practice in any community may be directly attributed to the influence of the hospital. It has been rightly said that the most valuable postgraduate studies the physician is ever likely to get will be found in the daily discussions of cases with his confreres in the hospital and in the more formal discussions at the staff meeting.

A good physician is, perhaps unconsciously, a good teacher. He passes knowledge he may possess on to his colleagues and, in turn, receives information from them. No one mentality can hope to have and retain all that is known in medicine, but by pooling this knowledge real progress may be made. This reciprocal teaching is, in the main, informal teaching but, none the less, it is teaching and should be productive of far-reaching results. The staff meeting is the most effective place for this.

A good physician has at least a modicum of what we call the scientific urge. It may be quite dormant, perhaps imperceptible, but usually it is present in some slight degree and responsive to the proper

stimulation. Oliver Wendell Holmes once said he attended church "because he had a little plant in his heart called Reverence which needed watering about once a week." Many a dormant quality such as the scientific urge could be cultivated by attendance at a hospital staff meeting once a week.

The smaller hospital in which all specialties participate jointly in the staff meetings has a definite opportunity in continuation education, provided the programs are teaching in character. This does not require any elaborate set-up or extensive financial outlay. For some years at the Thayer Hospital we have been endeavoring to carry on such a program in a necessarily modest way. Meetings are held weekly throughout the year, with the exception of eight weeks when the meeting is omitted in order to join with the County Medical Society in its monthly meeting. The programs are definitely teaching in character, consisting largely of case studies, selected from the hospital material. In addition we have reports from the different national and sectional society meetings, clinicopathological discussions, panels on pertinent subjects, and occasionally a guest speaker of repute. In the course of a year, with the proper selection of material, a fairly comprehensive program is presented. In this, otolaryngology plays an important part, together with the other specialties. Through these programs an effort is made to acquaint the clinician—both the general practitioner and the specialist—with a proper conception of the most important aspects of otolaryngology and of the otolaryngological phases of other disease conditions, largely from the viewpoint of diagnosis. These meetings are open to the profession and are attended by a number of physicians other than the staff, many coming from places 50 or 60 miles distant. In my opinion this is teaching quite as valuable as the formal courses, and provides an effective program of continuation education. I am not citing this as anything unusual or especially remarkable. I know it can be duplicated and far surpassed by other institutions. I am giving it as an example, with which I am personally familiar, of what can be done in a very simple way but with quite far-reaching results. I do feel that if some such scheme were more universal, our standards of clinical practice would be markedly improved.

#### OTOLARYNGOLOGY IN A PROGRAM OF CONTINUATION EDUCATION

Otolaryngology has a definite place, a mission to fulfill, in this program of continuation education. Much of the unfortunate results in medicine are due to sins of omission. Too often the otolaryngologist sees the end-result, the effect of undiagnosed conditions,



in cases first seen by the general practitioner. We all recognize the disastrous results of the neglected acute otitis media. The rapidly increasing popularity of chemotherapy with the resultant use of sulfanilamide and like drugs, indiscriminately and without proper control, adds to the problem. In this connection may I digress for a moment to suggest that education is a better preventive than chemotherapy? Since this program has been in effect we have had almost no cases requiring mastoid operation from the men in our own group. Cases of otitis media are referred for treatment as soon as seen. The cases requiring operation, almost without exception, come in from outside. I am sure our figures are quite as favorable as those where sulfanilamide has been used. One might say it's luck, but you can't make luck cover ten years. Perhaps the outstanding example of unrecognized and neglected emergencies is the case requiring tracheotomy. In my own experience this is the one real emergency, not outranked even by hemorrhage, when called away in consultation. Too often these patients are *in extremis* when seen. Better education of the general practitioner in these and many similar conditions is urgently needed and should be a distinct responsibility of otolaryngology.

This is not a responsibility solely for those who have made teaching a career. Let those who are teachers, in a formal way, continue with the work of training for the specialty and with the so-called refresher courses. And let those on the periphery, away from the formal teaching of the centers, assume the obligation for the informal education of the general practitioner in the needed phases of otolaryngology and for providing the stimulus to keep the younger otolaryngologists interested in continuing their education after the five-year momentum has been lost.

#### SUMMARY — EVERY HOSPITAL A TEACHING HOSPITAL

We must admit the necessity of a program of continuation education if the available medical service is to be satisfactory, if scientific medicine is to be practiced throughout the country. In order to make this effective it must be decentralized in order to reach the greatest number. The hospital has already proven to be the most effective force for improving standards of practice in any community. It would seem possible to develop gradually the plan of the teaching hospital so that the community hospital becomes something more than an agency for renting beds and rooms for the physician to practice therein whatever medicine he chooses. By becoming in fact a teaching hospital, not only will the interests of the patient be

further safeguarded but the standards of practice will inevitably be improved. This envisions regular staff meetings, definitely teaching in character, the fostering of proper reading habits on the part of the staff, and encouragement of staff members to attend meetings of the national and sectional scientific societies, to visit other clinics and teaching centers, and to take needed postgraduate courses. In all this otolaryngology has a distinct part, not by segregating itself into a separate department nor by leaving all instructions to those engaged in formal teaching, but by active participation in this educational program.

#### PROFESSIONAL BUILDING.

LXXVIII

THE FUNCTIONAL PATTERN OF THE AUTONOMIC  
NERVOUS SYSTEM\*

DAVID HIGBEE, M.D.

SAN DIEGO

The medical profession has a very usable knowledge of the sensorimotor nervous system by which many clinical phenomena are comprehended. There is no difficulty in understanding the mechanism of response to irritation, trauma and infection by the recognition of hyperesthesia, pain and rigidity. The status of these indicates the condition of the reflex arc in terms of normal, accentuated activity or paralysis.

It cannot be said that we have a comparable knowledge of the mechanism and symptomatology of the autonomic nervous system. There is however in this an anatomical structure and physiological response as definite as in the sensorimotor system.

As clinicians our interest centers around the manifestations of abnormal function in the various structures of the body.

It is my purpose to consider the general functional pattern of the autonomic nervous system and to present its symptomatology. To accomplish this without confusion of thought or the necessity for memorizing nerve tracts we need only comprehend its structure and apply basic laws of the conduction of stimuli in nerve tissue. Reference will be made to embryology and anatomy only in so far as it serves the purpose of telling us what this system is, how it works and what it does.

Certain conclusions are to be made, and it will add to our interest and understanding if they are stated at this time.

1.) The autonomic system is a part of the nervous system which presides over involuntary functions.

2.) It is divided into two portions. One, known as the sympathetic, regulates our adjustments to external environment. The

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\*Presented before the Western Section of the American Laryngological, Rhinological and Otological Society, San Francisco, Calif., February 2, 1941.

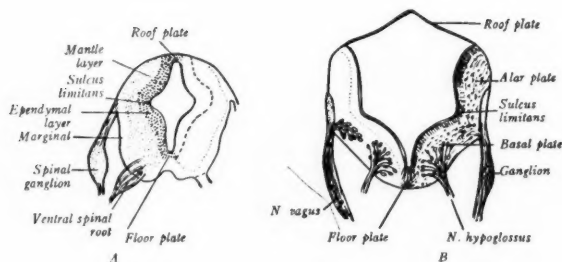


Fig. 1. Transverse sections of the neural tube showing the arrangement of the alar and basal lamina: A, Through the upper cervical region of the spinal cord in a 10 mm. human embryo (after Prentiss); B, through the myelencephalon of a 10.6 mm. human embryo (after His).

other, called the parasympathetic, presides over the functions which are vital to our existence. Together their activities embrace the whole fabric of metabolism.

3.) This system is a motor or efferent system. It does not carry sensations of pain. Its fibers are distributed to gland cells and cardiac and smooth muscle of the viscera and blood vessels.

#### EMBRYOLOGY

The earliest embryological distinction between the autonomic and the central nervous systems is not as clearly shown for the human embryo as it is for some of the lower vertebrates. In these, distinct masses of cells come off the posterior root ganglia and form the ganglionated cord. In mammals there is no migration of a cell mass. The separation occurs in small cell groups which are less distinguishable from the surrounding mesodermal tissues.<sup>1</sup>

There is however a well defined chain of sympathetic ganglia at the 7 mm. stage of the human embryo. At this stage the neural canal shows evidence of a division into dorsal and ventral columns. The neural canal becomes larger in the transverse diameter and there is a constriction of the nervous tissue surrounding it. This constriction is known as the *sulcus limitans* (Fig. 1A). On the dorsal side of this sulcus all the sensory nuclei of the brain stem and cord are developed and on the ventral side all the motor nuclei are developed. This arrangement of nuclei is present also in mixed nerves. The sensory and motor roots are each on their respective sides of the sulcus although close to the midline transversely (Fig. 1B).



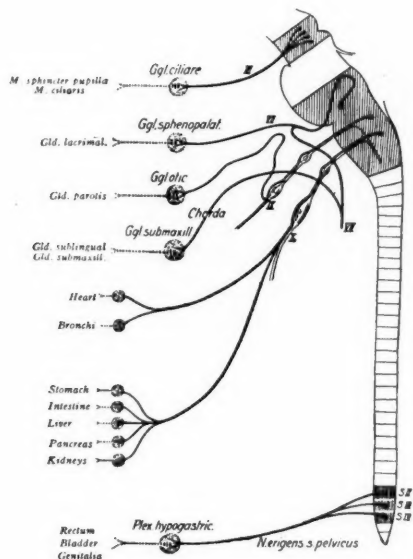


Fig. 3. The parasympathetic portion of the autonomic nervous system. Preganglionic fibers are indicated by continuous lines, postganglionic fibers by dotted lines.

#### ANATOMY

The autonomic system is divided into two main groups known as sympathetic and parasympathetic. Each has its characteristic anatomical structure and function. First we may consider the sympathetic or thoracolumbar division.

Figure 4 is a cross-section of the spinal cord. On the left side is shown the reflex arc of the sensorimotor system. On the right is shown the reflex arc of the sympathetic system. Sensory neurones have their cells of origin in the posterior root ganglion and carry sensations into the cord which are distributed through connector neurones to efferent tracts of both sensorimotor and sympathetic systems. The sensory neurones which come from the supporting tissues of the body are called somatic afferent tracts and those which come from the viscera are called splanchnic or visceral afferent tracts (Fig. 5). In the sensorimotor reflex a synapse with the connector neurone is made in the dorsal horn of the spinal column where its nutrient cell is located (Fig. 4). This connector neurone is short.

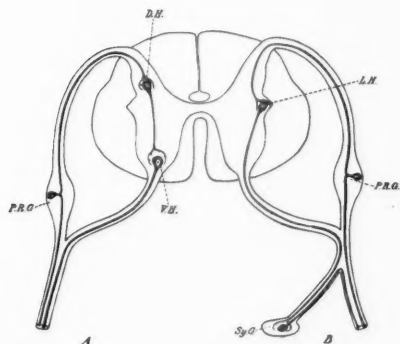


Fig. 4. A. The sensorimotor voluntary system. The receptor neurones run in the posterior root, their cells lying in the posterior root ganglia, P.R.G. The connector synapse neurones lie within the dorsal horn, D.H., and make with the effector neurones lying in the ventral horns, V.H., a synapse with the motor neurone, which emerges from the cord as the motor spinal nerve. B. The sympathetic nervous system. The receptor neurones run in the posterior root as a sensory neurone, making its first synapse in the cells of the lateral horn, intermedio lateral cell column, or *nucleus sympathicus*, L.H. The connector neurone runs out with the motor nerve as the white *ramus communicans*, making its synapse with the effector neurone in the sympathetic ganglia, Sy.G. The effector neurone runs in gray *ramus communicans* to the viscus directly.

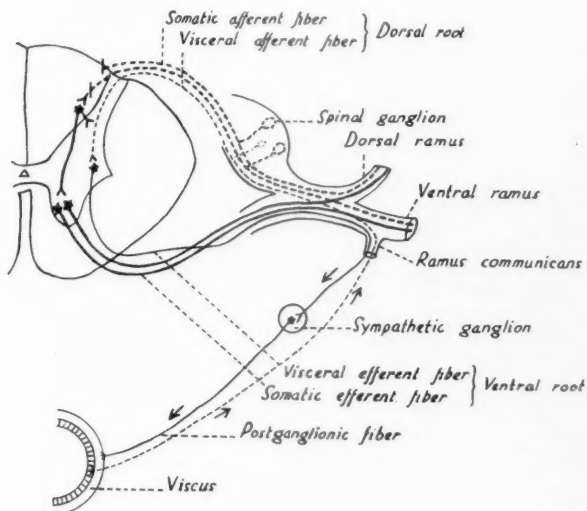


Fig. 5. Diagrammatic section through a spinal nerve and the spinal cord in the thoracic region to illustrate the chief functional types of peripheral nerve-fibers.

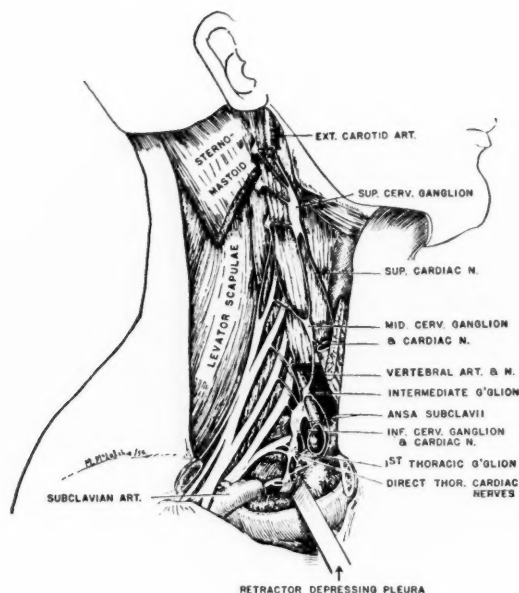


Fig. 6. The cervical sympathetic nerves.

It extends only to the ventral horn where contact is made with a nutrient cell of the motor neurone.

On the right side the afferent neurone ends in the *nucleus sympathicus* or intermedio lateral cell column where contact is made with a nutrient cell of the connector neurone. This connector neurone is long. It contacts a nutrient cell of the sympathetic ganglion by traveling through the mixed spinal nerve for a short distance. It carries a myelin sheath on leaving the cord and so is called the white *ramus communicans* but a more descriptive term is the pre-ganglionic neurone. After a synapse in the sympathetic ganglion the reflex arc is continued by a postganglionic neurone which extends from the ganglion back into the mixed spinal nerve and follows in the path of this nerve for final distribution (Fig. 4). The myelin sheath is lost in this synapse and so the postganglionic neurone is sometimes called the grey *ramus communicans*. A duplication of these ganglia superimposed upon each other extending from the first thoracic to the third lumbar vertebrae form the thoracolumbar or sympathetic portion of the autonomic system (Fig. 2). This



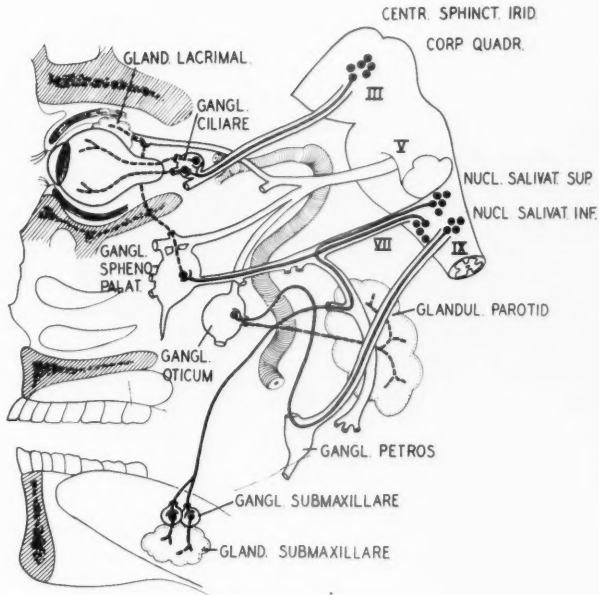


Fig. 7. Showing distribution of parasympathetic fibers and ganglia of the head.

arrangement of fibers applies only to the innervation of the trunk and appendages. There are also sympathetic components of the eight cervical nerves. They are fused into three ganglia known as the superior, middle and inferior. The first four nerves form the superior, the fifth and sixth form the middle and the inferior is made up of the seventh and eighth. This is the classical description although the middle ganglion is sometimes absent and the first thoracic is often fused with the inferior cervical to form the stellate ganglion (Fig. 6). Postganglionic fibers are attached to the carotid and vertebral arteries to gain their cephalic position and then join the efferent branches of the third, fourth, fifth, sixth, ninth, tenth and twelfth cranial nerves for final distribution.

The reflex arc is the functional unit of the nervous system just as the neurone is the anatomical unit. In the autonomic system as in the sensorimotor system the reflex arc is generally composed of a

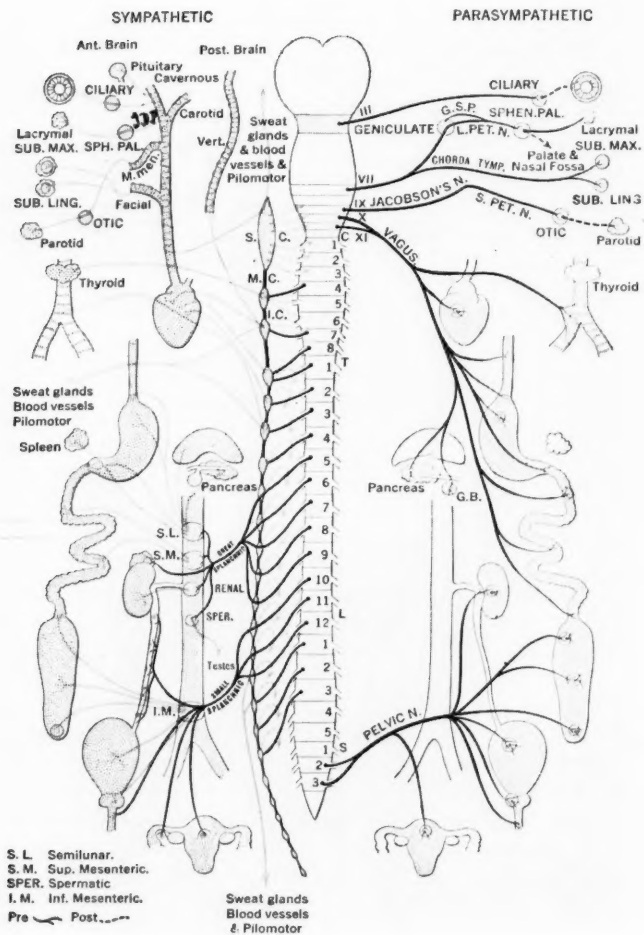


Fig. 8. Diagrammatic representation of the general scheme and distribution of the autonomic nervous system. The preganglionic fibers of the sympathetic and parasympathetic are in heavy black lines, postganglionic fibers of the sympathetic in light black lines and of the parasympathetic in dotted black lines.

sensory, a connector and an effector neurone. The first synapse in the sympathetic division occurs in the intermedio lateral cell column between sensory and connector neurones (Fig. 4). The second synapse occurs in the sympathetic ganglion between connector and effector or postganglionic neurones. The latter extends from the ganglion to the tissues which it innervates without further interruption (Figs. 2 and 5).

The parasympathetic division is composed of cells situated in three different levels of the central nervous system, *viz.*, the mid-brain, the medulla, and the sacrum (Fig. 3). It is characterized by ganglia which are located at relatively great distances from the cord in or near the tissues which they supply. They contact their respective third or effector neurones in peripheral ganglia by a distribution along the paths traversed by the third, seventh, ninth and tenth cranial nerves. Terminal distribution is by short effector neurones arising in the four great ganglia of the head, *viz.*, the ciliary, the sphenopalatine, the otic and the submaxillary, and also by the numerous visceral ganglia of the vagus where plexuses are formed in all tissues reached by this nerve (Figs. 3 and 7). The connector neurones of the sacral portion go directly to the pelvic ganglion, and effector neurones lie in the intrinsic plexuses of pelvic organs.

Such in general is the scheme of the autonomic structure by which the various organs are innervated by both sympathetic and parasympathetic nerves (Figs. 8 and 9).

#### PHYSIOLOGY

The role of the sympathetic division is that of an emergency mechanism. It does not act constantly and is not essential to life. (Cannon<sup>3</sup> has removed both ganglionated cords in cats and finds that if they are sheltered they live indefinitely. They grow normally and reproduce but are incapable of reactions incident to an independent existence.) It is stimulated through the special senses for the most part in adjusting man to his external environment. It is also stimulated by adverse conditions inside the body such as pain, hemorrhage, dehydration, infection and emotional states. This activity entails an extraordinary expenditure of energy which is accomplished by a discharge of adrenalin into the blood and the activation of sympathin at the myoneural junction. When stimulated the hair is erected, the pupils enlarged, the heart rate increased; blood pressure is elevated, the great splanchnic vessels are contracted, peripheral circulation is increased and sphincters are contracted.



The parasympathetic system functions constantly. Its role is to maintain a state of health within the body. It provides for the storing of energy and the reparative processes, and effects digestion and elimination. It is concerned with immunity and sensitivity. It presides over the activities of most of the endocrine glands. When activated it contracts the pupil, slows the heart, increases the tonus of the gastro-intestinal canal and empties the hollow viscera.





A summary of the reactions effected by these two divisions and the origins of their effector neurones is given in Table I.

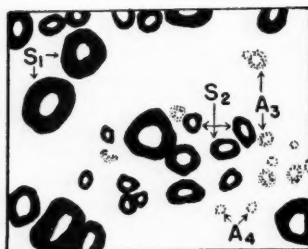
The stimuli which initiate these reflexes may arise from any one of the special sense organs and from biochemical or psychic states.

It has been known for more than one hundred years that an impulse can be conducted through a reflex arc in only one direction. In 1811 Bell showed that stimulation of the anterior roots caused muscular contraction. In 1822 Magendie found that stimulation of the posterior roots caused pain. These experiments preceded the nerve muscle preparation from which is learned that stimulation of the posterior root produces pain and contraction of muscle but that stimulation of the anterior root produces nothing but contraction of muscle. These facts form the basis of the Bell-Magendie law. The synapse is known to be the site of this directional mechanism and it must be considered as a gate which opens in only one direction.<sup>1</sup>

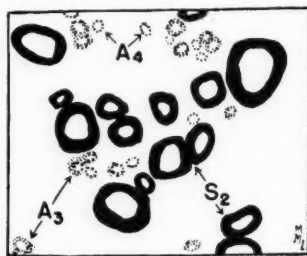
The law of isochronism supports the theory that sensations of pain are not conducted over autonomic fibers. By this we understand that between a muscle and its nerve there must be a similar reaction time inherent in these two tissues independently of each other. Lapique<sup>2</sup> has shown that whenever these reaction times differ by more than 100% the impulse is blocked. Heinbecker has studied the rate of conduction of stimuli in the various types of nerves. He finds the heavily myelinated fibers of the sensorimotor tracts will conduct stimuli at the rate of about 100 meters per second. The fiber tracts of the autonomic system which have little or no myelin will conduct stimuli at the rate of about 12 meters per second (Fig. 10).

So far one might infer that the autonomic system functions entirely as a segmental one without relationship to higher centers. This is true only in part. It must be regarded as a part of the whole nervous system and is neither wholly dependent nor totally independent of it. Many of these relationships can only be inferred but

TYPE	FORM	SIZE MICRONS	RATE M. PER SEC.	FUNCTION
S <sub>1</sub>		18-8.0	100.0 40.0	I. MOTOR TO STRIATED MUSCLE; TOUCH, PRESSURE & JOINT SENSE.
S <sub>2</sub>		6.0-3.0	30.0 15.0	II. PAIN, HEAT & COLD SENSE.
A <sub>3</sub>		4.5-1.5	12.0 4.0	III. MOTOR TO CERTAIN FASTER SMOOTH MUSCLES; CERTAIN PRE- GANGLIONIC SYMPATHETIC FIBRES.
A <sub>4</sub>		3.0-1.0	1.0 0.3	IV. VASOCONSTRICTORS & VASO- DILATORS; MOTOR TO BRONCHI & GASTRO-INTESTINAL TRACT.



HUMAN POPLITEAL NERVE



HUMAN MIDDLE CARDIAC N.

Fig. 10. Histological and electrical characteristics of different types of neurones. Type S<sub>1</sub>. Somatic—heavily myelinated axones—motor to skeletal muscle. Type S<sub>2</sub>. Somatic—medium myelinated axones—sensory to skin and viscera. Type A<sub>3</sub>. Autonomic—thinly myelinated axones—motor to viscera. Type A<sub>4</sub>. Autonomic—non-myelinated axones—motor to viscera. (Modified from Heinbecker, 1933.)

are nevertheless real. Evidence of psychic effects produced on the body as a whole are too numerous to mention. There is no joy, sorrow, rage, or shame that is not reflected upon the autonomic system. Although the cortical representation thus implied has not been defined anatomically it seems apparent that it must exist.

The influence of the cerebral cortex is manifested in many ways. Lesions of the cortex give evidence of vasomotor changes in those parts of the body related to the area affected. Shivering, sweating and gastro-intestinal symptoms are commonly caused by lesions of the cortex. Decortication experiments by Goltz<sup>6</sup> show the inhibitory influence of the cortex upon the hypothalamus. In the experiments of Cannon and Britton<sup>7</sup> reactions of the sympathetic system were

induced by stimuli which ordinarily would arouse no response and were greatly exaggerated and prolonged. There is strong evidence that centers for the control of sympathetic and parasympathetic reactions are located in the hypothalamus.<sup>8</sup>

#### PHARMACOLOGY

The actions of drugs can be classified by the reactions produced both at the synapse and upon the end organ. Some drugs affect only the sympathetic and others only the parasympathetic. The parasympathetic division is stimulated by insulin, choline, acetylcholine, pilocarpine and eserine. It is paralyzed by alkaloids of the atropine group and by nicotine. Sympathetic fibers are stimulated by those glands of internal secretion which have an affinity for chromium, *viz.*, the adrenal medulla and the thyroid and also by ephedrine and benzedrine. The motor and secretory fibers are paralyzed by ergotocin and ergotamine but not the inhibitory fibers (Fig. 10). Nicotine paralyzes all fibers of the autonomic system.

Experiments which offer a comparison of the effects of autonomic stimulation and the actions of certain drugs indicate that acetylcholine is the mediator between nerve ending and end organ in the parasympathetics and that sympathin plays the same role in relation to the sympathetics.

The activities of the sympathetic and parasympathetic systems are in general antagonistic effecting a balance poised to swing in favor of the immediate needs of the individual. The responses however are such that under normal conditions the parasympathetics maintain the function of vital organs at a constant level but under stress the sympathetics become dominant.

There are many legendary syndromes which implicate the autonomic system. Generally these are known as sympathetic neuralgias. In rhinology sphenopalatine ganglion neuralgia is an example, and there are equally well known sympathetic neuralgias in every special field. All of these are denied in this functional pattern. Sphenopalatine ganglion neuralgia has been on several occasions discredited by experimental and clinical evidence. The term persists in our literature despite abundant evidence to the contrary. The so-called cocaineization and injection of the sphenopalatine ganglion are impossible to accomplish. In these procedures it is the fifth nerve which is equally blocked if the pain is relieved. The fibers of the fifth nerve and those of the autonomic system are so intermingled

at the site of the ganglion and the sphenopalatine foramen from which they both emerge into the nose that one could not cocaineize one without equally affecting the other. The sphenopalatine ganglion is so small and so difficult to reach that a paraganglion injection is all that could be accomplished, in which case the fifth nerve fibers are equally affected.<sup>9, 10, 11</sup>

Whenever pain is a symptom it must be attributed to somatic or visceral sensory fibers. No autonomic afferent neurones have ever been found.<sup>12</sup> Each afferent neurone makes contact with many connector neurones, some of which are distributed to effector neurones supplying structures under volitional control and others to effector neurones supplying structures over which we have no control. By this multiple distribution of sensory fibers a diffuse response involving both voluntary and involuntary motor tracts may result from a stimulus perceived through a single sense organ.

#### SUMMARY

An explanation of the fundamentals of the autonomic nervous system has been presented. The background of embryology and anatomy has been reviewed so that the functions of this system might be clearly comprehended. The subject is too vast for great detail where space is limited.

Attention is called to the large amount of research which has established facts that clinicians in all specialties are often ignoring.

There is in our literature a firmly established symptomatology implicating the autonomic nervous system which should be revised.

3245 FOURTH AVENUE.

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TABLE I

ORGAN	PARASYMPATHETIC EFFECTS	ORIGIN OF AUTONOMIC POSTGANGLIONIC FIBERS	SYMPATHETIC EFFECTS
Heart	Inhibition	Superior middle and inferior cervical ganglia	Acceleration
Vessels:			
Cutaneous		Various vertebral ganglia	Constriction
Muscular		Various vertebral ganglia	Dilatation, Const.
Coronary	Constriction	Cervical ganglia	Dilatation
Buccal mucosa		Superior cervical ganglion	Dilatation
Cerebral	Dilatation	Superior cervical ganglion	Constriction
Abdominal and pelvic viscera		Prevertebral ganglia	Constriction
External genitalia	Dilatation	Prevertebral ganglia	Constriction
Eye:			
Iris	Constriction	Superior cervical ganglion	Dilatation
Ciliary muscle	Contraction	Superior cervical ganglion	Relaxation
Smooth muscle of orbit and upper lid		Superior cervical ganglion	Contraction
Nictation membrane (cat and dog)		Superior cervical ganglion	Retraction
Bronchi	Constriction	Thoracic ganglia	Dilatation
Glands:			
Sweat		Vertebral ganglia	Secretion
Salivary	Secretion	Superior cervical ganglia	Secretion
Gastric	Secretion	Celiac ganglion	Inhibition?
Pancreas			Secretion of mucus
Acini	Secretion	Celiac ganglion	
Islets	Secretion	Celiac ganglion	
Liver		Celiac ganglion	Glycogenolysis
Adrenal		No postganglionic fibers	Secretion

TABLE I (Continued)

ORGAN	PARASYMPATHETIC EFFECTS	ORIGIN OF AUTONOMIC POSTGANGLIONIC FIBERS	SYMPATHETIC EFFECTS
Smooth muscle:			
Of skin			
Of small intestine	Increased tone and motility	Vertebral ganglia	Contraction
Of large intestine	Increased tone and motility	Celiac and superior mesenteric ganglia	Inhibition
Of bladder wall	Contraction	Inferior mesenteric and hypogastric ganglia	Inhibition
Of trigone and sphincter	Inhibition	Inferior mesenteric and hypogastric ganglia	Inhibition
Of uterus, pregnant		Inferior mesenteric and hypogastric ganglia	Contraction
Of uterus, non-pregnant		Inferior mesenteric and hypogastric ganglia	Contraction
			Inhibition

Resume of autonomic effects and origin of postganglionic neurones. Note that secretion, constriction and dilatation are functions of both.

## LXXIX

### EXOPHTHALMOS\*

A. D. RUEDEMANN, M.D.

CLEVELAND

The patient who comes in with a protruding eye or "pop-eye" presents a difficult problem for everyone concerned in the diagnosis. The problem usually is a painstaking one and requires deliberation. By gradual exclusion of all the factors, several possible diagnoses may be arrived at, the final diagnosis being absolutely certain only when the mass, or tumor, or the orbit has been cut into and the tissue is examined.

Certain features of exophthalmos should be considered before anything else is taken up. First, exophthalmos should be divided into two types: (1) the bilateral type, and (2) the unilateral type.

Bilateral types of exophthalmos are limited to general disease. A tumor rarely arises in both orbits at the same time or in the neighborhood of the orbit with sufficient growing power to push out both orbits at the same time. Therefore, one can almost immediately exclude the cases of bilateral exophthalmos by saying that as a rule they are due to general disease. If the case is bilateral, usually the ophthalmologist must be concerned with the general health of the patient—pulse, blood pressure, blood counts. However, both eyes should be measured with an exophthalmometer in order to determine definitely whether or not both eyes are exophthalmic.

Frequently a unilateral exophthalmos occurs, the fellow eye appearing wide open because of the drooping of the other lid, or because of an effort of the individual to maintain normal single vision.

After ruling out all cases of bilateral exophthalmos as being due to general disease, the congenital orbital defects and the congenital globe defects from other orbital pathology must be differentiated. In cases of unilateral maldevelopment, one orbit may be shallowed out and the globe pushed forward. However, in most instances this also is bilateral, either as a full grown case of oxycephaly or one of its many modifications, which may be confusing the diagnosis.

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\*Presented before the Eastern Section of the American Laryngological, Rhinological and Otolological Society, Philadelphia, Pa., January 10, 1941.

As mentioned previously, cases of exophthalmos due to trauma are now seen more frequently. It is well to mention here also cases of unilateral exophthalmos secondary to orbital trauma. When the integrity of the orbital cavity has been broken or interfered with, subsequent atrophy of the orbital tissue produces an exophthalmos. Associated with this may or may not be a widening of the bridge of the nose, depending upon how the case was treated at the time of injury or immediately after the injury. A great deal can be done for orbital injuries at the time of the injury. However, so little usually is done that a secondary orbital atrophy with an enophthalmos results. Enophthalmos is very disturbing to the patient and, unless both eyes are measured, the fellow eye may erroneously be considered exophthalmic.

The history and roentgen examination will reveal the change in the size of the orbit. However, it must be remembered that the cases of exophthalmos are diagnosed by exclusion of other factors. It also occurs in a large buphthalmic or myopic eye, and with megalophthalmos a diagnosis of exophthalmos may be made because of the extreme increase in the size of the globe. This is ruled out easily by comparing this eye with the size of the fellow eye.

Protrusion of the eye may be produced either by compression of the orbital cavity by outside pathology, or the orbital content may be increased by local tissue reaction or by new growth. It seems that it would be rather easy to exclude the possibility of new growth pushing into the orbit from the outside, or surrounding pathology producing sufficient change in the bone to compress the orbit. However, this is not always easy to diagnose, as is well demonstrated by a patient whose history is described in this presentation.

It is important to remember that the orbit is completely occupied at all times by the eyeball, muscles, fat, nerves, vessels, blood volume, and a certain amount of lymph. The eyeball cannot be pushed back into the orbit; therefore, because of the nature of the surrounding territory, the only direction the eyeball can go is forward. It also must be remembered that a considerable amount of new orbital tissue is required to move the eyeball forward one millimeter. Although the eyeball comes to a cone apex posteriorly, anteriorly it opens and flares out wide. Therefore, to move the eyeball forward one millimeter, a volume increase of the orbit of approximately 1600 cubic millimeters is necessary. This must be borne in mind when dealing with orbital tumors or orbital pathology, as physicians are frequently surprised by the size of the ab-

scuss or the size of the local growth in the presence of only a small amount of exophthalmos.

It is also well to remember that intracranial pathological condition *per se* does not, as a rule, change the position of the eyeball except in very rare instances. It is certainly not true, as was stated in a paper recently, that encephalitis may depress the eyes by increased intracranial pressure with secondary pressure upon the orbit. The position of the eyeball is changed later in life only by a muscle paralysis as far as intracranial pressure changes are concerned. When changes in the position of the eyeball do occur with increased intracranial pressure, the diagnosis is so obvious that differentiation is not necessary.

The cases of unilateral exophthalmos are of importance to the otolaryngologist because he is one of the important differential diagnosticians in this condition. His help is sought in every case in which this diagnosis is made and frequently his help is required during surgical maneuvers. Again, cases of unilateral exophthalmos may be divided into two groups, and there are definite differences in the etiological factors of these two groups.

In children, certain sinuses are absent up to seven and eight years of age. Certain low-grade diseases in the orbit that are not seen in adults, as a rule, may be found. For example, tuberculous periostitis is rare in adults, but not so uncommon in children. Exophthalmos secondary to hemorrhage is not uncommon in children, especially in the white children who are afflicted with scurvy. Here again, however, evidence of the disease is found elsewhere in the body, such as inflammatory or injected knee joints and, in general, the picture of malaise.

Exophthalmos in children should definitely be divided into two groups: (1) the inflammatory group, and (2) the noninflammatory group. Although a sharp demarcation cannot always be made, this division definitely helps in classifying the types of lesion. If it is inflammatory, the sinuses must be excluded immediately or the possibility of an orbital cellulitis or abscess secondary to some general condition. Any previous constitutional disease may produce or lead to an orbital abscess.

It is well to remember that it is not advisable to enter the orbit with a knife unless it is absolutely necessary. The diagnosis governs the incision to be made. It is possible to take a large bore needle on a tight syringe and enter into the posterior orbit to find a possible abscess cavity or some other lesion which can be drained through a

needle, or at least a differential diagnosis can be made. However, probing in the orbit is not recommended as a routine procedure in the differential diagnosis. Surgical procedures should be undertaken only after all other measures have been tried. When the integrity of the orbit has been disturbed, the subsequent functional result is in direct proportion to the amount of maneuver that has been tried or done within the orbital cavity.

An inflamed prominent eye in a young child always leads to some trouble posterior to the eye, but does not always mean that the orbit must be entered in order to make a diagnosis or give treatment. This is especially true in the cases of orbital edema with some stasis of the blood due to involvement of the ethmoid or the antrum in which poor drainage from the nose is present. In these cases, especially if the clinical diagnosis of antral or ethmoidal disease can be made, the patient should be put to bed and given supportive measures, such as frequent applications of heat to the face, drops to the nose, and suction to establish drainage through the nose. A surprising number of these youngsters never need orbital surgery. The eyeball will go back into position without the disfiguring scar from orbital invasion and its subsequent lack of good functional movement.

A draining sinus from the orbit does not always indicate osteitis or periostitis. I well remember a draining sinus of the superior part of the orbit in a youngster five years of age. The history was incomplete and the roentgenogram revealed no definite change in the bone. While probing along the sinus, we came upon the remains of a lollipop stick a good inch in length. It had entered the orbit when the youngster had fallen upon the stick while running. The fall had been of sufficient severity to blur the youngster's memory of what happened to his lollipop, and the stick had been in the orbit long enough to produce a draining sinus with a considerable amount of granulation tissue around the piece of wood.

The temperature, blood counts, roentgen examination, and nose and throat examinations of the individual all are extremely important in the cases of unilateral exophthalmos with inflammation.

In the noninflammatory groups in children, an intermittent exophthalmos may be present due to a vascular tumor of the orbit that has pushed the eyeball slightly forward. In the upper inner corner of the orbit there may be either a thinning of the nasal wall or a dehiscence due to an encephalocele. Here the diagnosis is aided by roentgenographic study because of dehiscence of the bone that

usually occurs in this area. New growths within the orbit usually consist of either dermoid cysts with associated keratomatous changes or hemangiomas. Sarcomas are seen rarely in children insofar as the orbits are concerned, and carcinoma has not yet been seen by us.

Every possible diagnostic point must be investigated in order to determine the etiological factor in unilateral exophthalmos, whether it be inflammatory or noninflammatory. At the present time we have a youngster in the hospital probably with undulant fever. No other cause for her difficulty can be found. She has bilateral exophthalmos, more marked in the right eye than in the left eye. The eyeball was pushed straight forward, showing that the tissue was well in the posterior orbital space, and the entire orbital content was moved forward as a mass. The amount of protrusion varies from time to time and, although there is a possibility of this being an orbital abscess, treatment with deep roentgen therapy and diathermy has reduced the exophthalmos several millimeters without anything else having been done. Nothing of significance has been found in the general condition of this youngster except that she presents a very strongly positive reaction to undulant fever. Associated with this is a fever reaction during the day which makes us suspicious that we have the proper diagnosis.

The position of the eye aids in the differential diagnosis. Lesions invading the orbit from without or surrounding areas, usually push the eyeball into position opposite to the invaded area. This is not always exactly correct because a tumor may grow in the posterior orbit and, because of lack of space in the orbital cavity posteriorly, it may slide up over the eyeball and push the eyeball inferiorly and appear as a superior orbital tumor.

Unilateral exophthalmos occurring in adults requires considerable study before a definite diagnosis can be established. All otolaryngologists, of course, are aware of the spontaneous exophthalmos that occurs in patients who have a dehiscence of the bone on the nasal side and in whom a strong sneeze or a hard blowing of the nose suddenly produces an exophthalmos. This, as a rule, is accompanied by air going into the orbit and into the lids. If the finger is rolled across the lid, crepitation or a feeling of air moving under the finger is noticed. This is not an uncommon accident, and a light blow upon the orbit may produce sufficient injury to the nasal bony wall of the orbit, which is not very strong, and the patient may have a dehiscence, as has been noted in many instances.

Everyone has seen cases of sudden exophthalmos following the washing out of the antrums under pressure in which the tip of the



cannula has been forced beneath the floor of the orbit. This usually is not a serious accident. However, it could be serious because of the accompanying pus that may be forced into the orbit with the contents of the wash. This rarely ever occurs in the well-trained otolaryngologist's office. However, in teaching institutions where younger men are being taught to wash the antrums through the natural openings and have not yet learned the delicacy of touch, they are apt to force the cannula and, in attempting to use the opening produced, they also force the fluid with subsequent protrusion of the eyeball.

Roentgenograms do not always show definite lesions in the orbit as there may be a dehiscence of the bone posterior to the orbit which is not shown. This is demonstrated in the case of a woman who came in with a slight degree of exophthalmos of a year's duration. The roentgenogram was entirely negative. Physical examination, however, revealed that this woman had a low-grade frontal sinusitis, and the diagnosis of orbital abscess was made. In going into the orbit by way of the frontal sinus, which was full of pus and granulation tissue, a large posterior orbital abscess was found with an opening about the size of a dime into the bone. This entire process, however, was so insidious that the patient was not aware of her exophthalmos except that she had a definite loss of proper functional movement of the muscles of both eyes. The diagnosis was made on clinical evidence alone, and the procedure was carried out because the frontal sinus showed evidence of dropping well down over the posterior aspect of the orbit.

It is important to remember that acute and noninflammatory orbital edema is associated with angioneurotic edema and other allergic factors, and also is associated with the early stages of trichinosis. Edema occurs even before the eosinophile count is raised.

New growths appearing in the orbit of an adult may be inflammatory or noninflammatory. The sarcomas are usually non-inflammatory and usually come down into the orbit from above or occur in the largest percentage, at least 75%, in the superior half of the orbit. They usually are well encapsulated growths and, as a rule, can be removed *in toto*.

An entirely different picture is presented by the carcinomas of the orbit. Most metastases in the orbit reported have been secondary to carcinoma, these arising almost anywhere in the body. Orbital carcinomata are usually infiltrating new growths, produce pain, are inflammatory, and tend to early fixation of the globe. It is well to

remember that they usually come from the antrum or the nasal side of the orbit, and are unilateral as a rule. This is particularly distressing because of the pain and early fixation of the globe, and the orbit must, as a rule, be exenterated.

By measurement of both orbits in one patient, it was found that she had bilateral exophthalmos. She had a very high pulse rate of 120, and a subsequent basal metabolism test showed her basal metabolic rate to be plus 87%. We were sure that she had this inflammatory reaction of the eyeball from the exposure of the globe. The muscle paralysis was due to a weakness of the inferior rectus and the lateral rectus. This is rather unusual in cases of exophthalmos due to hyperthyroidism because the superior rectus usually is involved first, the lateral rectus secondarily, and the inferior rectus only rarely.

It might be well to mention here the cases of pulsating exophthalmos, which are not rare. The history is not always very definite and the expected bruit is not always present. It may be transitory, both to the patient and to the examiner. Until the advent of the automobile, most cases of pulsating exophthalmos were secondary to spontaneous rupture of a vessel within the orbit, trauma playing a very minor role. However, these cases now are usually traumatic in origin, being due to automobile injuries. Every case of exophthalmos should be listened to with a stethoscope for a diagnostic bruit. By gradual elimination of all the diagnostic factors, a fairly safe diagnosis can be arrived at in most cases of unilateral exophthalmos. However, this is not always possible and the physician need not feel the least bit chagrined to be wrong at the time of operation.

Pseudotumors of the orbit in adults are not uncommon, arising usually from a posterior ethmoidal cell. The entire orbit is invaded by low-grade granulation tissue which usually is painful, inflamed and insidious in growth.

Panophthalmitis is another inflammatory process occurring in the orbit. It arises from the anterior portion of the socket and is usually so obvious that no difficult diagnostic point is involved, except occasionally as in the case of a patient having a panophthalmitis subsequent to a rupture of a corneal abscess, which in turn was subsequent to an exophthalmos produced by hyperthyroidism. This hyperthyroidism was so severe and serious that we could not remove the eyeball until after the patient had had a thyroidectomy and treatment. Here again, watchful waiting in the presence of active hyperthyroidism was just as dangerous as watchful waiting can be

in orbital lesions. The best functional result is always obtained by early diagnosis and treatment.

#### SUMMARY

1. Exophthalmos is extremely distressing to the patient and is very difficult to diagnose.
2. The diagnosis should be made early and surgical intervention directed at the source within the orbit to produce the best functional result.
3. The diagnosis is made by exclusion only. It requires painstaking study in every instance.
4. Examination of the nose and throat is necessary in every patient with a protruding eye.
5. Roentgenograms are a great help but are not to be relied upon entirely.
6. Although surgery is the method of choice in most instances, the integrity of the orbit should be maintained as long as possible, and the operation of choice should be the operation that will produce the best functional result insofar as movement of the eyeball subsequent to surgery is concerned.

CLEVELAND CLINIC.

THE USE OF PRESERVED HUMAN CARTILAGE IN  
RECONSTRUCTIVE FACIAL SURGERY\*

SAMUEL IGLAUER, M.D.

CINCINNATI

From time to time various substances have been implanted into facial or cranial depressions which have resulted from the loss or displacement of underlying bone or cartilage. Among the materials which have been introduced to restore the contours, both inorganic and organic substances have been used, including metal plates, cork, paraffin, celluloid, ivory, fat, fascia, bone, and cartilage. In the course of time from the experience of many surgeons it was found that while some of these materials remained as quiescent foreign bodies, others underwent partial absorption, while still others excited suppuration or pressure necrosis and were extruded.

In general it may be stated that the more nearly the implanted substance resembles or is biologically related to the tissues of the host, the more certainly will it remain in its new environment. At the present time there are three tissues commonly employed as implants for the restoration of facial contours, namely, ivory, bone, and cartilage.

## IVORY

The use of elephant ivory for the correction of the saddle nose has been advocated by Joseph,<sup>1</sup> Maliniak,<sup>2</sup> Salinger,<sup>3</sup> Wolfe<sup>4</sup> and others. These authors all state that ivory usually remains as a permanent implant and seldom excites any marked reaction in the surrounding tissues. Nevertheless, in Maliniak's series of 68 implants, four required early removal because of infection, and three had late removal because of pressure necrosis. In Salinger's 50 cases, the ivory was removed in nine instances for various reasons, including primary infection (four cases), spontaneous extrusion (one case), and trauma (four cases). Disregarding the cases due to trauma, it will be seen that in the experience of each of these two

\*From the Department of Otolaryngology, College of Medicine, University of Cincinnati. Presented at the Middle Section meeting of the American Laryngological, Rhinological and Otolological Society in Chicago on January 27, 1941.

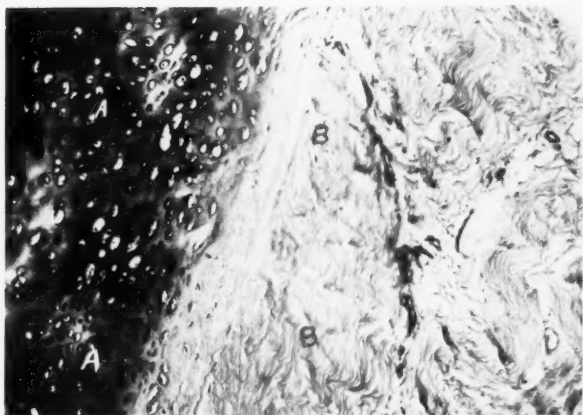


Fig. 1. Section of autocaltilage removed from subcutaneous tissue of abdomen nine years after implantation. *A*—Essentially normal tissue except for areas where cellular spaces are more numerous than usually seen. *B*—Fibrous connective tissue intimately adherent to cartilage.

authors about 10% of the implants had to be removed, and it is apparent that a definite result cannot be anticipated with the use of ivory and that its routine use is contraindicated.

#### BONE GRAFTS

Autogenous bone grafts have been used by many surgeons, including Joseph,<sup>1</sup> Carter,<sup>7</sup> Kazanjian<sup>6</sup> and others, to fill in depressions of the face and skull. The advantages of bone lie in its rigidity where support is required and its ability to resist strain and to form a union with contiguous bone. Since grafted bone requires a blood supply for its survival, it is more prone to infection than cartilage which can draw its nourishment from the tissue juices. For these reasons bone grafts are only occasionally used in reconstructive surgery of the face.

For the correction of saddle nose deformity Cohen<sup>7</sup> considers the use of a combined piece of autogenous bone and cartilage, taken from the osteochondral junction of a rib, preferable to either bone or cartilage used singly. He states that if the rib bone is brought into contact with the nasal bones, firm union will take place, thus fixing the graft in its new environment.

## AUTOCARTILAGE

The implantation of autoplasic costal cartilage for the correction of saddle nose deformity was first employed by Nélaton in 1900.<sup>8</sup> In a comparatively short time it became the favorite material, since it is readily obtainable, easily modeled, after implantation requires no special blood supply of its own, and is resistant to infection. Experimental studies by Peer<sup>9</sup> and others have demonstrated that fresh autogenous grafts of human cartilage survive as living tissue after transplantation and that histologic examination of the cartilage many months after its transfer reveals no marked change in the structure of the specimen. In this connection I have sections of autogenous cartilage removed from patients, respectively, thirteen, nine, and four and a half years after implantation. The oldest specimen showed only slight degenerative changes in viable cartilaginous tissue. The nine-year specimen showed well-preserved and apparently viable cartilage (Fig. 1). The four and a half year specimen showed the matrix intact, but the majority of cells were absent. Some large areas, however, showed striking degenerative changes with eroded and crumbled cartilage (Fig. 2). This case represents an exception to the general rule.

Despite its virtues, the chief objections to the use of costal autocartilage are its failure to form a firm union with contiguous bone, the unpredictable tendency of cartilage to curl upon itself, and, above all, the necessity of subjecting the patient to a painful and confining operation. In fact, the postoperative complaints of the patient focus on the rib and not upon the nasal operation. Furthermore, in the case of young athletic persons it is inadvisable to weaken the thoracic cage.

## PRESERVED CARTILAGE

In the latter part of 1938, following the favorable report by O'Connor and Pierce on the use of "refrigerated cartilage isografts,"<sup>10</sup> I began using cartilage preserved according to their method. In this paper I wish to report briefly my experience with this material.

*Preparation of Cartilage.* Rib cartilage is removed from the cadaver, is stripped of its perichondrium, washed in water, and introduced into a sterile glass jar containing aqueous merthiolate (1:1000), one part, and sterile normal saline, four parts. The cartilage should be well-covered by the solution to insure penetration of the fluid. The container is placed in a refrigerator for three days, when the solution is poured off, a fresh solution added, and refriger-



Fig. 2. Photomicrograph of autocaltilage removed from nose 4½ years after implantation. A—Essentially normal cartilage. B—Degenerated cartilage showing fragmentation. Note absence of cellular infiltration.

ation continued. After a week the solution is again changed, after which it is ready for culturing. O'Connor and Pierce take cultures of the supernatant antiseptic fluid before each operation. I prefer removing bits of the cartilage, washing them thoroughly in normal salt solution, and culturing the tissues for 48 hours. If they are found to be sterile, cultures are not taken prior to each operation but at longer intervals.

I should add that the collection of the cartilage requires close cooperation between the pathologist and the surgeon. It has been our practice to avoid cartilage from subjects presenting evidence of acute infection or of malignant disease.

The cartilage will keep *in vitro* indefinitely, is pliable, resists fracturing, is easily modeled, and does not curl after implantation.

*Surgical Technic.* In the operating room in order to minimize the possibility of contamination, one surgeon models the cartilage at a side table while the other prepares the recipient bed which should be just large enough to receive the graft. In correcting a saddle nose a midcolumellar incision is usually employed, avoiding the anterior nares which are difficult to sterilize. In other parts of the face the incision is made at some distance from the actual depression so that the sutures will not come in contact with the graft. A molded

lead splint, held in place by an elastic band, is applied over the graft to prevent the formation of a hematoma and to retard the swelling.

#### REPORT OF CASES

About two years ago I began using merthiolated isocartilage in plastic reconstruction of the face. I have employed this method on 25 patients with excellent results in all but two cases. In the first case, that of a patient with a deformed syphilitic nose and a three plus Kahn reaction, the graft was extruded. In the second case suppuration occurred, but the graft remained *in situ* after incision and drainage. In the follow-up I have received satisfactory reports on 22 cases from one week to 21 months after operation. Among these there were 12 cases of traumatic saddle nose deformity, four cases in which slivers of cartilage were implanted to restore alar or other minor defects, three cases in which a bow-shaped piece of cartilage was implanted into the upper lip for the relief of dish face, and one case in which two superimposed pieces of cartilage were implanted to fill up a depression of a malar bone. The latter case was interesting inasmuch as the second cartilage disc was inserted over the original implant seven months after the first operation. Some of the other cases were of especial interest.

The patient, C. R., was a boy, aged 17, with a traumatic saddle nose deformity due to a septal abscess. At his first operation I inserted a piece of autcartilage which had to be removed on account of infection. Three years later I inserted a piece of ivory through a midcolumellar incision, but this had to be removed on account of pressure necrosis. Fourteen months after the second operation a piece of preserved rib cartilage was implanted and has remained in good position ever since, that is, for 17 months.

In the case of C. P., a boy, aged 13, with a traumatic saddle nose deformity caused by a septal abscess, I implanted a piece of autcartilage in 1931. In 1940, when the patient had reached manhood, his nose appeared too flat, so that a second piece of preserved cartilage was superimposed on the original graft with an excellent surgical and cosmetic result.

In the case of E. S., two slivers of preserved cartilage were implanted through marginal incisions in the alae to relieve inspiratory collapse of the nostrils.

In another patient who had a nasal autograft, additional slivers of preserved cartilage were introduced on two different occasions to improve further the cosmetic appearance.

Two patients presented themselves with implanted autcartilage which had curled up, producing a secondary deformity of the nose. In one of these the cartilage was removed, reshaped, and reinserted. In the other, a piece of preserved cartilage was substituted for the original implant.

In each of two patients having a flat nose and a dish face deformity, a piece of L-shaped cartilage was introduced into the dorsum of the nose with the long



arm of the "L" under the dorsum and the short arm implanted in the mobile septum. A good result was obtained.

*Fate of Implanted Preserved Cartilage.* From the clinical experience of O'Connor and Pierce,<sup>10</sup> Straith,<sup>11</sup> and myself, among others, implanted merthiolated human cartilage remains *in situ* without any clinical evidence of absorption or distortion. However, in a recent article Peer<sup>12</sup> reports on some experimental studies with human cartilage preserved in alcohol and subsequently implanted beneath the skin of other human beings. The first reaction noted was a collection of giant cells, polymorphonuclear leucocytes, and round cells about the foreign body, with the subsequent formation of a connective tissue capsule about the implant. After about a month this reaction disappeared, and the cartilage remained unchanged as tolerated dead foreign material for about ten months. Sections removed after this period showed some progressive invasion of the implant by fibrous tissue and partial absorption of the cartilage.

In evaluating Peer's experiments it should be stated that there may be a difference between cartilage pickled in alcohol and that preserved in merthiolate. The alcohol has a dehydrating effect, while the merthiolate produces the fixing effect of a mercury compound. Furthermore, it should be remembered that the effects noted are minimal and microscopic compared to the bulk of cartilage implanted, and as pointed out by Peer himself, the substitution of fibrous tissue for the cartilage does not necessarily nullify its value as an implant (except perhaps in skull defects).

I should like to add that if in the course of several years the implant should become reduced in size, it would be a very simple matter to introduce a new or an additional piece of preserved cartilage to supplant the loss.

#### SUMMARY AND CONCLUSIONS

1. As judged by a statistical study, the ultimate fate of implanted ivory is uncertain, and routine use of this substance in reconstructive surgery of the face is contraindicated.

2. Autogenous bone grafts may be used but do not "take" as well as cartilage.

3. Autocartilage is an ideal material for implantation and survives for many years.

4. The necessity of subjecting the patient to a rib operation constitutes the chief objection to the use of autcartilage.

5. Human cartilage preserved in aqueous merthiolate is an excellent substitute for both ivory and autcartilage.

6. A brief account is given of the author's experience with preserved cartilage.

7. The employment of preserved cartilage simplifies the operative technic and minimizes the necessity for hospitalization of the patient.

I desire to express my appreciation to Dr. Philip Wasserman for his study of the histology of the tissues and to Dr. M. Herzberg for culturing the material.

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THE RELATION OF GERIATRICS TO  
OTOLARYNGOLOGY

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The purpose of this study is to clarify the meaning of geriatrics and stimulate a new interest in the otolaryngologic care of the aged. An effort will be made first to present the general picture and recent history of geriatrics with the pathological and medical background. As much of the voluminous literature has been empirical and scientific laboratory research still incomplete, this must largely be a collaboration, but nevertheless essential for understanding.

The coining of the word geriatrics to cover a special branch of medicine dealing with old age, was claimed by Nascher,<sup>1</sup> and used by him in a paper which appeared in the New York Medical Journal in 1909.

Stieglitz,<sup>2</sup> in charge of investigations in gerontology by the National Institute of Health, differentiated "gerontology, the problems of old age" from "geriatrics, the diseases of the aged and consequences of senescence." He divided the problem of aging into three major fields: (1) biologic, as a process; (2) clinical problems of aging and diseases of advanced age; (3) socio-economic problems of shifting age distribution. Physiologic age is not synonymous with chronologic age, and senescence cannot be measured by chronologic age.

With amazing rapidity has interest in the field of geriatrics, which seems to have been introduced but yesterday, spread over the entire medical world, heralding a new science devoted to the medical, sociologic and economic welfare of the older group of people.

Perhaps the most informative thing which has appeared from the standpoint of the medical profession has been proof of the decreasing birth rate, the diminution of the youthful group, and the enlargement, under protecting conditions of health, of the aging

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<sup>1</sup>Presented in part before the Virginia Society of Ophthalmology and Otolaryngology, May, 1941.

group. Pediatrics bids fair soon to become less and geriatrics more absorbing of medical attention. In our own department of otolaryngology, both surgeons for the aged and aged surgeons will doubtless unite in studying geriatric medicine from its practical angle.

#### HISTORICAL REVIEW

The field of geriatrics cannot be adequately portrayed without a brief review of its history. It has been claimed that the subject of geriatrics obtained interest even long before the classic oration of Cicero on old age. Piersol,<sup>3</sup> Bortz<sup>4</sup> and others have noted, as of historical interest, the great achievements in literature, art and music, by people of advanced age.

The recent wave of enthusiasm seems to have reached a certain crest around 1939, when Cowdry's<sup>5</sup> "Problems of Aging: Biological and Medical Aspects," published under the Macy Foundation, appeared. In this review some 25 leading scientific men discussed every phase of biologic, physiologic and psychologic aging, with discussions of the elements involved.

Notable presentations were made by Warthin<sup>6</sup> in 1928, and recently by Boaz,<sup>7</sup> Kennedy<sup>8</sup> and Piersol<sup>3</sup> in connection with the New York Academy program.

It should not be inferred that contributions of value were too localized. In this field some of the finest fundamental work in studies of degenerative changes have been done in widely separated geographic areas. Advances in matters which concern civilization would seem to progress historically in waves, with surges of interest culminating in localized major movements. A particularly fine culmination of this work occurred in the symposium on the problems of old age, presented at the recent bi-centennial of the University of Pennsylvania. Surgical aspects were discussed by Brooks<sup>12</sup> of Vanderbilt University, statistical and social implications by Dublin<sup>13</sup> of the Metropolitan Life Insurance Company, involuntional changes in the cardiovascular system by Karsner<sup>14</sup> of Western Reserve University, and medical aspects by Pepper<sup>15</sup> of the University of Pennsylvania. These extensive reviews should render a real service to this group which may soon aggregate 22,000,000 persons.

Interesting statistics have come to light in these recent surveys. The average duration of life of the ancient Roman citizen was from 20 to 30 years. Life expectancy at the end of the 17th century had

only advanced to 33.5 years. In Sweden between 1755 and 1776, the mean length of life was only 34.5 years. A decade after the Declaration of Independence, the mean length of life in this country was only 35.5 years, and in 1850 life expectancy in New England was but 40 years. By 1900 longevity had increased in the United States to 48 years, by 1930 to over 60 years. The studies of Dublin estimated by projection that in 1980 (40 years hence) only 26% of the population would be under 20 and that those over 45 would include more than 40% of our people.

It is most interesting to contrast these facts, as suggested above, with such noted examples as Lord Balfour on active duty at 72, Sarah Bernhard't performances at 70, Cato's studying Greek at 80, Goethe's completing Faust in his 80th year, and the fact that some of Verdi's greatest music was written and Edison's greatest accomplishments made when they were over 80. Titian's greatest pictures and Stradivarius' finest instruments were produced in their ninth decades. To these examples may be added Judges of our own Supreme Court, leading contemporary international figures, and perhaps even carefully matured otolaryngologists.

#### A REVIEW OF MEDICAL AND SURGICAL OPINIONS

From the physiologic and pathologic standpoint, Piersol<sup>13</sup> has pointed out that from the embryonic life to death, involutionary processes occur in four groups: (1) numerical atrophy (loss of the power of cell division); (2) quantitative atrophy (reduction in the size and number of parenchymatous cells); (3) shrinking and condensation of the intercellular substance; (4) vascular changes (vessel collapse and obliteration of the lumen).

Diseases of old age tend toward degenerative conditions such as a chronic heart disease, chronic nephritis, arteriosclerosis, angina pectoris, cerebral hemorrhage, diabetes mellitus and cancer.

Karsner<sup>14</sup> has maintained that involution or retrogressive changes in aging were distinct from diseases appropriate to age. In studying the principles of wear and tear, one does not customarily find the counterpart of the destructive effects of friction in living organisms. Many of the phenomena called wear and tear may be but end results from deteriorative processes initiated by infection. In 400 autopsies, Aschoff found no deaths attributed solely to old age, and none was recorded in 19,000 autopsies on people of varying age at Western Reserve University.

These valuable studies by Karsner and others of the cardiovascular system have left the impression that there are but few alterations which are unquestionably due to involution. It is not clear how much may be the result of previous infection, hemorrhagic changes, traumatism in early life or other factors not strictly retrogressive.

Boas<sup>7</sup> has faced the problem in "Aging of the Cardiovascular System" with the utmost frankness. He raises the question as to what organic bodily changes are the result of the inevitable involution of tissues and organs and what are the results of environmental and accidental factors. The answers to such questions would determine the direction of scientific study of senescence and the therapeutic approach to persons suffering from so-called degenerative diseases commonly regarded as the phenomena of aging.

Arteriosclerotic lesions in very elderly patients have been demonstrated by autopsy as not being consistent. Evidences of senescence such as loss in height, loss in weight, presbyopia, graying of hair and loss of skin elasticity, are none of them disease processes nor challenge continuance of life. Likewise some changes in the circulatory organs seem to signify aging but not disease, such as pigmentation, calcification and diabetes.

Moore<sup>16</sup> has recently classified the neurologic conditions occurring after 50 years of age and notes that "when those diseases which ordinarily occur in the earlier decades of life make their appearance after age 50, the symptoms and signs are frequently altered or so different as to cause many commissive and omissive errors in diagnosis; second, among the vascular and degenerative diseases, some of the commonly anticipated conditions may simulate, disguise or occur concurrently with other disease entities not usually suspected."

Pepper<sup>15</sup> has expressed the opinion that geriatric progress has been delayed by too much emphasis on mere longevity, and feels that our goal should rather be health in old age. While senescence is physiologic aging, he finds it interesting to speculate on future views. While death is inevitable, it may occur without many changes today accepted as normal for advanced age, such as loss of teeth and hair, whitening of hair and *arcus senilis*, which future preventive medicine may overcome. He suggests crystallizing our hopes in some such phrase as "Delay senescence and avoid senility."

He quotes Draper's terminology in the statement that senescence occurs in each of the panels of personality, the anatomic, the physiologic and the psychologic. He cites vascular, epithelial, and atrophic

changes in almost all tissues and organs, with lessening of mass and weight of the brain, the kidneys, the endocrine and other glands. He emphasizes in the functional field the lowering of basal metabolism, impaired figures in kidney function, the disappearing of gastric acidity and the loss of peripheral reflexes.

Some three years ago he electrified his audiences by the statement that blood pressure and tobacco and alcohol moderation were not so much of consequence to the older man as unwise difference in marriage age and dietary indulgence. While old patients responded to surgery better than to medicine, nursing was more important than either. Medication should be guarded, particularly as to drug idiosyncrasies, obesity, strain. Maladjustments in marriage should be avoided; food intake should be 10% less and the chewing apparatus, the feet and the skin should be cared for.

Some authors, however, have observed that dietary restrictions in the aged are based on fear and habit rather than research.

Piersol<sup>12</sup> considered that the most helpful records of group studies on patients over 60 years of age came from the clinics of Barker and his associates. They reported that the chief complaints were referable to the nervous, digestive, circulatory and locomotor apparatus. There were relatively few whose outstanding symptoms suggested diseases of the respiratory tract, the blood itself, the urogenital tract or the endocrine glands. Cardiovascular disease, disorders of the nervous system and diseases of bones and joints occurred in that order of frequency.

Few have emphasized the diabetic phase more carefully than Bortz.<sup>17</sup> Diabetic individuals must avoid infection. If man be as old as his arteries, the first concern in disease is to work out the proper kind of diet, one which will aid in keeping the arteries elastic and resilient. In his ten rules as the "decatalogue of health," the first was to eat more fruit, fresh green vegetables and milk, and less starches, sugars, and heavy meats. The next emphasized elimination, fluid intake and deep breathing exercise. The remainder covered rest, undue worry, anger, cultivation of friendships, intellectual stimulation and wise reading. The more one contemplates such advice, the more appropriate it appears.

A study of the vitamins in relation to the ear, nose and throat, with careful review of the opinions and literature as to specific deficiency factors, was recently presented by Jones,<sup>18</sup> in whose opinion each vitamin has a preponderant effect on special structures derived from the ectoderm, mesoderm and endoderm. He enumerates the

origin of tissue groups in the upper respiratory tract and suggests specific vitamin importance to each. He emphasizes the fact that the defense mechanism requires in all tissues an adequate amount of vitamins.

Covell<sup>19</sup> found that Vitamin A deficiency in rats was associated with middle ear infections, changes in the periosteal layer of the otic capsule and exostoses in the internal auditory canal, as well as degeneration of parts of the organ of Corti. Deficiencies of Vitamins C and D registered the same changes. He noted that the muscles of the middle ear had fibrous replacement in the animal lacking Vitamin E intake, as well as hemorrhagic changes about the nerve of the modiolus.

Probably no one has contributed more on the surgical side than Barney Brooks,<sup>20</sup> with his elaborate tables on the results of surgery on patients of advanced age. These included a group of operations on otolaryngologic patients in the higher age groups. Certain surgical procedures were rendered justifiable by the reasonable expectation of producing more favorable readjustment in the ear, nose and throat tract. In reviewing a group of 293 operations on patients over 70 years of age, he noted that surgical diseases in the higher age groups showed a relatively high mortality, but the deaths which could reasonably be attributed to operative treatment were infrequent.

From a clinical standpoint, surgery may be attempted in an aged person with far more security than before believed. Modern pre- and postoperative care justify what would have seemed impossible 25 years ago; gentle administration of anesthesia either local or general has removed harsh force from the control of the patient; the preliminary measures of safety in laboratory analysis of various sorts and the varied kinds of anesthesia have made the process relatively simple. While one can not escape the fact that healing is slower (indicated by de Nuöy<sup>21</sup> as "six times as slow in the aged"), it is nevertheless comparatively safe. A hemorrhagic condition can be studied in advance and controlled; tissues in an older person are not as sensitive and the shock of operative trauma is less. On the other hand, the absorption of the products of major surgery is slower and the after recovery must take a longer period. It is a delicate question as to whether the limit of necessary surgery should be attempted.

It is very interesting to note Dr. Brooks' speculation upon the effects of shift in the age composition. In general the obstetricians



and pediatricians could anticipate a diminution in the number of births and of children; internists could look forward to an increase in the incidence of degenerative diseases; general surgeons could look for an increase in their responsibility because of later incidence of surgical disease; the urologists would be busy with a larger group of old men, but the gynecologists would probably not be seriously overworked with their even larger group of old women; ophthalmologists might look forward to performing many operations for cataract, but the otolaryngologists would do relatively few operations on the ear, the nose and the throat to compensate for the decrease in tonsillectomies and adenoidectomies; the orthopedist was already aware of the decrease in tuberculosis; the neurologic surgeon might expect an increase in the number of tic operations and the plastic surgeons, more reconstruction after epitheliomata but fewer operations for harelip and cleft palate. The internist's function would assume greater proportions. It would devolve upon him to determine proper preparation of these aged patients for the combination of trauma, drugs, confinement, strange environment, irregularity in nutrition and emotional upset constituting a surgical operation.

#### SPECIAL RELATION TO OTOLARYNGOLOGY

The relation of geriatrics to otolaryngology would obviously concern conditions of a certain chronicity rather than acute reactions of temporary character and equally obviously would eliminate cancer, tuberculosis and specific disease. These groups represent factors in aging, but they are incident to any age, and medical and surgical therapeutics must be subject to each age limitation.

In a clinical study of degenerative influences in maturity, it is clear that routine otolaryngologic care and physiologic readjustment are inseparable. A review of the popular article by Gray<sup>22</sup> on the mystery of aging will be convincing.

Otolaryngologists in this field must be expert in laboratory conclusions, internists of no mean ability and psychoanalysts as well as surgeons, or at least in coordination with such expert assistance. Fortunately those experienced in the care of the aged have advanced far in their knowledge of the biochemic changes in tissue maturity, have realized the variability in age standards and lines of demarcation.

The criticism by Pepper of the undue emphasis upon longevity instead of health in old age has already been quoted. In harmony

with this thesis, health must represent not only physical comfort but a mental acceptance of that physical comfort.

On the physical side, the maintenance of that health in the upper respiratory tract involves many fundamental factors: the balance of intra- and extra-cellular fluids, stimulation and guarding of lymphatic defences, dietary and medicinal compensation for deteriorating salivary, gastric and intestinal secretions, counterbalancing the inevitable tendency to atrophic change, and the study of circulatory imbalance, endocrine deficiency, and dehydration.

Cowdry,<sup>23</sup> in discussing the progressive impairment of the regulatory devices of homeostasis of the blood in relation to different tissue fluid environment as old age creeps on, alludes to these important changes:

- a. Decrease in metabolic rate.
- b. Decrease in ability to store and use glucose.
- c. Reduction in alkali reserve of the blood.
- d. Increased blood pressure.
- e. Aging of colloids.
- f. Progressive dehydration and other changes.

On the mental side belongs the management of the inevitable personality changes occurring in aging patients, stimulating the desire to live and be healthy. Very suggestive is Hamilton's<sup>24</sup> analysis of factors causing feelings of inferiority and general inadequacy in aging persons, as in part simple reaction to declining physical vigor, loss of occupation, the calendar and the traditional assumption of what old age inevitably involves.

This enumeration of opportunities for tuning up physical and mental deficiencies should spur the specialist to corrective effort on fundamental defects which routine topical treatment will never reach.

Three fields in otolaryngology for the aged would seem to invite rather special consideration.

1. *Elimination of toxic foci*: Principally this refers to teeth, sinuses, Waldeyer lymphoid tissue, middle ear or distant trouble in the intestinal tract and prostate. It would be trite to more than discuss the surgical phase. It is the consensus of those who seem to know that while response to medicine is poor, response to surgery in the aged patient is good, with, as Brooks<sup>12</sup> states, the increasing knowledge of most appropriate methods to be used in meeting the

peculiar combination of trauma, receipt of drugs, confinement in strange environment, irregularities in nutrition and emotional upset, constituting a surgical operation.

2. *Correction of mechanical block to drainage and aeration:*

It would seem unfair to permit an elderly person to be carried along so many years when almost-minor surgery would bring about an anatomic readjustment. This, of course, refers particularly to the fields of rhinology and the middle ear.

3. *Otologic complications in progressive deafness:* Otology of the aged presents three pictures of interest:

a. Disturbances in the external ear, canal and auricular integument.

Management of disturbances of the external auricular canal, whether simple eczematous, herpetic, fungoid, or intermittent furuncular in aged people, is as important as the care of the teeth, feet, and skin cited earlier in this article. Although not pathologically critical, these conditions cause a sufficiently constant nervous irritation, even at an age when pain is less acute, to undermine physical well-being. Therapeusis here is difficult because of poor response to any local medication; in fact, general physiologic deterioration is so much involved that it becomes a biochemic problem.

b. The long continued middle ear discharge of chronic otitis media.

Infection of the middle ear may involve all its component parts, the eustachian tube, the middle ear and the mastoid. Whether the theories of infantile tympanic changes in relation to pneumatization of the mastoid be accepted or not, the role of squamous epithelium in relation to cholesteatoma forces the otologist to a cautious study of the different types of tympanic perforation in planning his middle ear campaign—that of the lateral wall, especially productive of cholesteatoma, that of the central, rather automatic in its self determination, and that of the attic, a true geriatric problem if it occurs in the neighborhood of the stapes.

c. The somewhat baffling symptom-complex of progressive deafness.

The symptom complex of progressive deafness presents the most striking picture of age deterioration in the whole field of otolaryngology and the somewhat striking analogy to the cataract and fundus changes of the ophthalmologist.

The writer<sup>25</sup> recently discussed the growing and somewhat courageous tendency to clarify three types of progressive deafness: (1) conductive, the property of the component parts of the middle ear; (2) the progressive osseous change in the labyrinthine capsule, termed otosclerosis; and (3) changes in the cochlea and perceptive apparatus, usually degenerative. These might be schematically visualized as anterior conductive, middle otosclerotic, and posterior nerve degenerative.

Consensus of opinion has established rather definite etiology for these three types: conductive deafness (including the adhesive and retracted middle ear)—infection in the nasopharynx and eustachian tube; otosclerosis—familial transmission, toxemia, infections of adolescence and the pregnancy complex; perceptive or internal ear deafness—traumatism and neurologic influence from the higher centers.

Otosclerosis has not been solved and perhaps should not be placed in geriatric study. If of familial type it commences in a younger age but affects the geriatric, and it still offers the grandest field for research. The first group invites help even in the aged.

#### CONCLUSION

It is probable that the larger percentage of aging patients will come under the care and direction of the more matured and experienced otolaryngologists. These clinicians probably will have become more conservative in their views, less ready to adopt the newer therapeutics, and perhaps less courageous in surgical procedure and its responsibility. They will, however, maintain the confidence of the mature patient, their operative work will be done with more care and less traumatism, their judgment should be keener, their study of the surrounding clinical conditions and surgical preparation should be more exacting.

Upon the surgical side, the writer feels that much more surgery in older patients could be safely attempted, when neglected or acute cases present, and these patients will be more ready today for any justifiable operation than they were ten years ago. Present developments have released them from much apprehension in regard to biochemic, hemorrhagic and anesthetic complications. Their cooperation, however, must depend upon the physician's ability to maintain the patient's psychic equipoise and his will to live.

An eminent specialist in another field recently discussed with a group of young medical friends the general trend in medicine today.

After reviewing changes over a course of years, he maintained that future successful medicine would combine but two great fields, first, preventive medicine, and second, priestcraft in medicine. Nothing could apply more appropriately to the care of the aging patient in our specialty and his occasional necessary surgery.

The increasingly aged group is with us, a period of life which demands the most refined art in medicine, rare diagnostic experience, skillful therapeutics and, again emphasized, rare judgment as to justifiable surgery in otolaryngology.

1912 SPRUCE ST.

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LXXXII

THE ORGANIZATION OF THE JOSEPH C. BECK  
HEAD AND NECK TUMOR GROUP

A GROUP COMPOSED OF INDEPENDENT SPECIALISTS INTERESTED IN THE  
DIAGNOSIS AND TREATMENT OF HEAD AND NECK TUMORS

JOSEPH C. BECK, M.D.

CHICAGO

WITH THE COLLABORATION OF

F. J. NOVAK, JR., M.D., L. B. BERNHEIMER, M.D., S. A. FRIEDBERG,  
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F. B. QUEEN, M.D., ERIC OLDBERG, M.D.

DIVISION OF CHIEF CONSULTANT

Specialization has and is progressing in all walks of life to such an extent and with such speed that it is very difficult at times to keep up with it. Medicine is no exception, and in the field of oncology (tumor science) we are pleased to place on record the organization of a group of independent specialists interested in the diagnosis and treatment of head and neck tumors. It is our hope that this will meet with the approval of the majority. We desire to have the recognition of this special field within the specialty of tumors as a whole. The group limits its endeavors to neoplasms of the head and neck and to those affecting the broncho-esophageal regions.

Each of the individual specialists will in the following pages describe his duties in the working of the group. Future groups desiring to follow our plan may pattern their organizations accordingly. There are accompanying this article two figures showing the group formation that we follow. This however, is so constructed that it may be modified to suit other groups both in large and small localities. Through unification of purpose, through cooperative efforts of the individuals in the group, we hope to achieve for the benefit of the patient the best possible diagnosis and treatment of neoplastic disease in the head and neck region. The research problems studied will represent all the phases of tumor work. The end

result of treatment will be critically scrutinized by the entire group so that where differences of opinion exist regarding the selection of surgery or irradiation, some fair conclusions may be drawn.

This group has selected Doctors Joseph C. Beck and Frank J. Novak, Jr. to act as chief consultants. We serve not as dictators, but rather as mediators and consultants in the whole field.

The group works with all three types of patients—private, semi-private and charity. The referring physician who sends his patient to the group for diagnosis or treatment or both is assured of having his patient referred back to him during and after treatment. It is only on the recommendation of the referring doctor that patients are accepted for treatment. The management of these patients is in no way affected by their social or economic status, except as to smaller details such as housing and nursing care.

One of the most important activities of the group is its regularly scheduled meeting or conference. Here patients are presented before, during and after treatment for the purpose of discussion by the group and by visiting physicians. Statistically, we are in possession of clinical records, photographs, and gross and microscopic pathological material of several hundred neoplasms, which we plan to present at a later date.

Because a knowledge of the general condition of the patient is important in the diagnosis and treatment of the neoplastic disease, it is necessary to have available the services of a competent internist who furnishes a complete clinical and laboratory report of the general organism. The report can, of course, be furnished by the family physician or general practitioner, providing he has the necessary facilities for clinical and laboratory work.

The importance of a secretary and social service worker cannot be overemphasized. This individual is responsible for recording the discussions at all meetings and for the management of the follow-up system. Having the necessary social service data, she may ethically request a patient to return for follow-up examination after treatment. Careful follow-up work makes possible complete statistical analyses.

Such groups should be centrally or conveniently located for the convenience of both patient and doctor. The specialists comprising this group are members of the various tumor clinics in Chi-



cago. It is our aim eventually to centralize head and neck tumor material in one place.

In addition to the chief consultants, the personnel of the group is made up of the following divisions: 1) otolaryngology, 2) ophthalmology, 3) oral and plastic surgery, 4) neurosurgery, 5) radiotherapy, and 6) pathology. Non-medical members of the group are the physicist, the recording secretary and the social service worker, the photographer and the laboratory technicians.

#### DIVISION OF OTOLARYNGOLOGY

The treatment of head and neck malignancies has undergone marked revision during the past few years, primarily due to improvement in radiological technique and to modernization of radiological armamentarium. Tumor specialists who are trained essentially in radiotherapy have made marked inroads into the field of otolaryngology. These specialists have had limited surgical training, hence are often unsympathetic with the otolaryngological surgeon, and as a result many controversial problems have arisen. The solutions to these problems are obviously important and can be obtained only through close, unbiased cooperation between radiotherapist and surgeon. Such a relationship may best be achieved through group studies of head and neck neoplasms, groups composed of both surgeons and radiotherapists. The otolaryngologist plays an important role in such an organization, having three principal functions: diagnostic, therapeutic, and educational.

The otolaryngological members of the group must have fundamental training in neoplastic diseases. They must have an understanding of any tumor occurring from the vertex of the skull to the diaphragm, whether these tumors be primary in origin or the result of distant metastases. The otological and rhinological aspects of intracranial neoplasms, the obscure symptomatology of early malignancy in the nasal passages, nasopharynx, larynx, trachea, bronchi, and esophagus — all offer a challenge which may be successfully met only through painstaking examinations, study and intelligent interpretation. These men must be prepared to obtain biopsy specimens from easily accessible lesions as well as those available only through endoscopic instruments or through the surgical exploration of paranasal sinuses, mastoid, nasopharynx and soft tissues of the neck. The judicious use of evidence afforded by roentgen rays, with or without opaque media, must be understood. Soft tissue roentgenographs of the neck and planography may greatly enhance knowledge regarding the extent of neoplasms when properly interpreted.

The efforts of the otolaryngologist will be required in the surgical management of head and neck malignancies, both with the cold knife and electrocoagulation. He will be called upon to perform partial or total laryngeal extirpation, block neck dissection, lateral pharyngotomy and other major surgical procedures as well as to cooperate with the radiotherapists of the group in the implantation of radium needles, radon seeds or radium moulds. These cooperative efforts are most important as they should lead toward increased efficiency in a field where partiality toward the surgeon or the tumor specialist has been previously unavoidable. Furthermore, in many instances, opportunities will be available for adherents of different views to display their wares. As examples: can the roentgenotherapist offer an 85% rate of cure for early intrinsic non-infiltrating carcinoma of vocal cords? If he is able to demonstrate this per cent of five-year cures, he will have proven that this form of cancer may be as well treated by roentgenotherapy as by laryngofissure. Is there justification in the enthusiasm for total laryngectomy in treating intrinsic infiltrating laryngeal cancer? Is the belief true that such lesions do not respond to irradiation? Can carcinoma of the pharynx and antrum be controlled most successfully with electrocoagulation, irradiation or a combination of the two? These and similar questions will be studied and re-examined by the group.

It behooves the otolaryngologist to spread the gospel of early diagnosis. The limitations of tumor therapy at the present time are chiefly those imposed by the extensive character of most neoplasms when seen for the first time. The routine microscopic examination of nasal and aural polypi can be shown to lead toward an earlier recognition of neoplasms in these regions. Commonplace nasal or aural symptoms may be those of early nasopharyngeal carcinoma. Obscure pharyngeal complaints are daily disregarded when their significance is highly important. Hoarseness and dysphagia cannot be too greatly emphasized as warnings of potential gravity, and it should be borne in mind that direct examination of the larynx reveals obscure pathology which escapes indirect examination with the laryngeal mirror. Not only the laity but the medical profession must be constantly re-impressed with these facts if any progress in successful treatment of malignancies about the head and neck is to be anticipated.

#### DIVISION OF OPHTHALMOLOGY

Tumors of the orbit and its adnexa constitute some of the most important diseases with which the ophthalmologist has to contend.

The vision and even the life of the patient may depend upon early diagnosis and treatment.

These tumors are infrequently seen in the average eye practice, and only ophthalmologists engaged in extensive clinical ward work have the opportunity to see many cases. There are, therefore, very few practitioners who are thoroughly familiar with the varying symptoms and findings present in such cases.

Tumors of the orbital adnexa, such as the lids, are usually referred to radiologists, who, due to their special training in radiology and lack of sufficient surgical experience, may be prejudiced in their form of treatment. The result is that recurrences are very frequent, and then considerable extensive plastic surgery is required to improve the condition present. Such difficulties could be easily avoided if the ophthalmologist were sufficiently well trained in the surgery required to remove such lesions. Excision of tumor growths and immediate plastic repair could be undertaken early, and then, if necessary, be followed by the radiotherapy deemed most suitable by a capable radiologist.

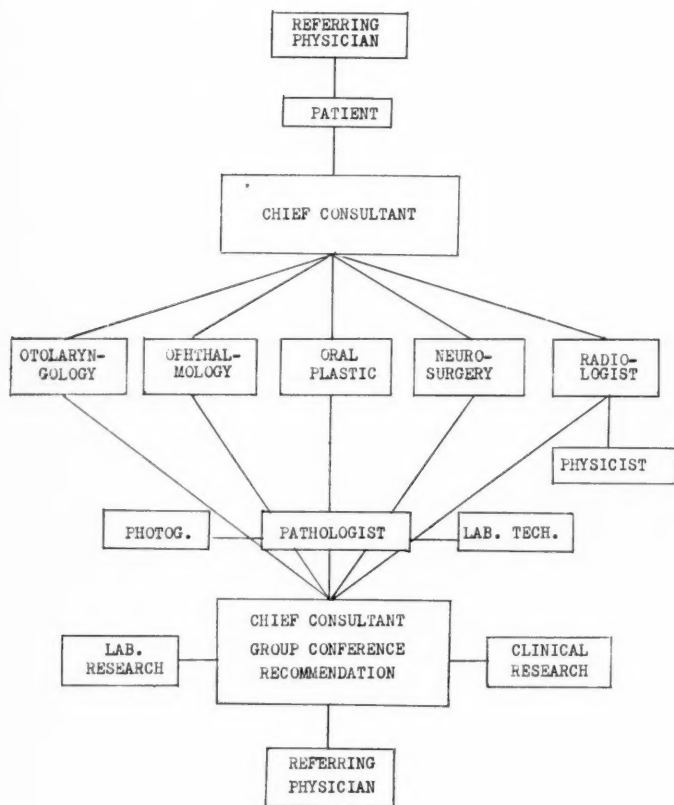
Such problems can be best handled by close, unbiased cooperation between radiotherapist and surgeon, probably working closely together in a group composed of head and neck surgeons and radiotherapists.

Cooperation between ophthalmologist and otolaryngologist is necessary in cases where intraorbital tumors may invade and break through the orbital wall and involve the accessory nasal sinuses. The reverse process may also occur, *viz.*, the invasion of the orbital wall by neoplasms originating in the nasal sinuses. The question may then arise as to the appropriate approach for surgical interference, whether from the nasal or orbital side. Here again, the advice of a competent radiologist may be necessary as to the proper form of therapy, namely, surgery or radiotherapy.

The ophthalmologist plays a necessary role in a head and neck tumor group, as the anatomy of the orbit is so intimately related to that of the accessory nasal sinuses that there are many problems of diagnosis and therapy which are common to both his field and that of the otolaryngologist. The radiologist should cooperate with both such specialists.

The radiologist may be able to advise radiological therapy in many problems encountered by the ophthalmologist where a tumor such as glioma may involve one remaining eye, and enucleation would

## DIAGNOSIS AND OPINION



result in total blindness. Here, appropriate radiotherapy may halt the malignant process and preserve useful vision. After tumor excision and plastic repair, some form of radiotherapy may be advisable. The proper therapy to be used is best dictated by the radiologist working with such a group.

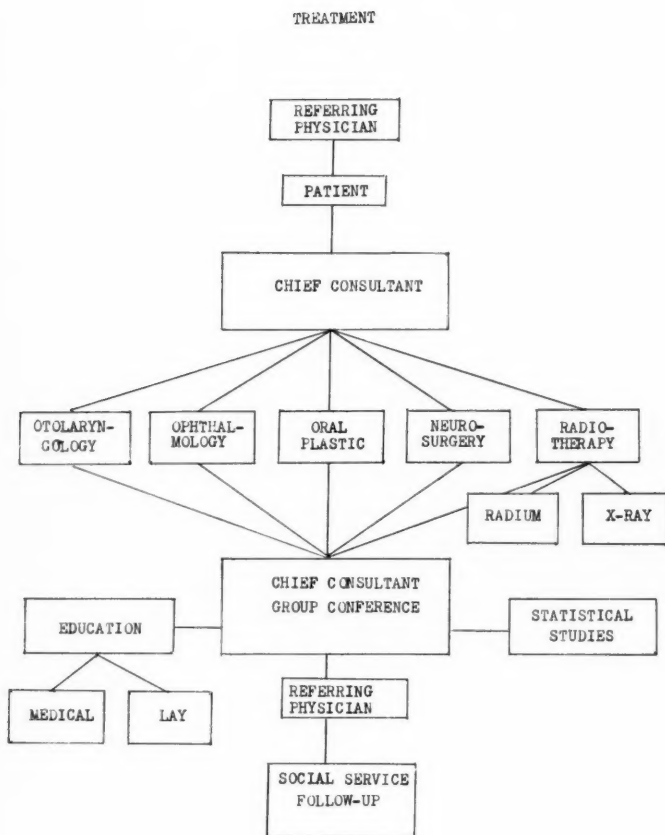
Tumors on the eyeball may require the implantation of radium needles, radon seeds, or a radium mould. This form of therapy is best advised by the radiologist. Such cooperative efforts lead to increased efficiency in the use of the best form of therapy, and friction or rivalry between the tumor specialist and the surgeon is thus avoided.

The ophthalmologist must impress upon his colleagues the importance of early diagnosis and therapy, especially in intraocular tumors. Early visual changes and flat localized retinal detachments must be recognized when first seen in their incipency. The tentative diagnosis of a tumor is then made and the proper therapy is executed. If one hesitates until marked intraocular changes are present, the patient's life is jeopardized, and enucleation or exenteration then fails to prevent metastases, which indeed may already be present. The surgeon must be able to recognize intraocular findings which are indicative of metastatic tumor involving the eye from some distant part of the body. This means careful, frequent and thorough ophthalmoscopic examinations.

It is only through close cooperation between ophthalmologist, otolaryngologist, oral surgeon and radiologist, working in complete harmony, that a successful head and neck tumor group can properly function.

#### DIVISION OF ORAL AND PLASTIC SURGERY

Working with a group devoting themselves to the problems of head and neck tumors, the oral and plastic surgeon finds himself in a position to contribute helpful cooperation by reason of his training in medicine, general surgery and oral surgery. In addition his knowledge of dentistry enables him better to appreciate and evaluate diseases of the mouth and jaws and to design and construct, if necessary, the appliances which may be needed in the application of therapeutic measures or to carry out prosthetic procedures often necessary to the successful eradication of disease, or in reconstruction when disease may have been eradicated. Many tumors occurring in the mouth and jaws such as cysts, odontomas, myeloid and giant cell sarcomas and some others, are not malignant. The oral surgeon



recognizes these tumors as such and can suggest the necessity for conservatism and the avoidance of mutilating operations.

One important function of the oral surgeon is to prepare mouths for X-ray or radium therapy. Attention has been directed repeatedly to the danger of irradiating the oral tissues where tooth or bone infections may be latent or likely to develop subsequent to treatment. Before irradiation is permitted, we feel that all devitalized teeth, all teeth showing evidence of pyorrhea, and all teeth which cannot be considered absolutely sound and healthy should be removed and the soft tissues allowed to heal completely.

The use of radium therapy about the head and neck often requires that adequate and well fitting molds and plaques be constructed. The implication is that molds do not merely hold the therapeutic agent in correct position but also properly protect adjacent structures. Molds fulfilling these requirements are best made by trained dental technicians from accurate impressions taken by the oral surgeon who will design and give instructions for mold construction.

Oral and facial prothesis will fall into the same plan. Relief of the emotional stress under which a patient with malignant disease labors may be attained by successful operations, but these operations are often of necessity radical. However, to cure disease and leave the patient to suffer perhaps greater physical and mental torture because of deformity is not an end to be desired. Prosthetic restorations are often the indicated or necessary answer to this problem.

Plastic surgery, however, has achieved a definite usefulness in the attack on malignant disease. The acceptable repairs which can be effected in this field are a definite boon to the surgeon who must be courageous and often ruthless when confronted with the necessity of destroying to cure.

#### DIVISION OF NEUROSURGERY

The neurological surgeon plays a somewhat subsidiary part in the head and neck tumor group, for the very great majority of his cases are entirely intracranial and, therefore, do not fall into the category of more or less external lesions with which the group is primarily concerned. There are several points, however, in which his field touches upon those of the other members of the group. Some of them may be briefly described as follows:

A number of neoplasms involving the head produce pain. The neurological surgeon may be called upon, therefore, to inject or divide the various branches or main trunks of the trigeminal and glossopharyngeal nerves.

Some tumors involving the nasopharynx invade the base of the skull and the intracranial cavity, producing basi-cerebral and cranial nerve symptoms. In these cases, neurosurgical consultation is of value, although roentgen therapy, as a rule, is the only method of treatment of any avail.

In lesions in and about the orbit and globe, the neurological surgeon sometimes collaborates with the ophthalmologist. Thus, exophthalmos may arise secondary to an orbito-ethmoid or orbito-sphenoid meningioma, which has intracranial significance in addition to the associated exophthalmos. In exophthalmos from intracranial aneurysm, the neurosurgeon may sometimes be called upon to tie the internal carotid and even occasionally to operate upon vascular lesions of the circle of Willis. The ophthalmologist also may see retinal angiomas, which have neurosurgical significance because of association with comparable intracranial lesions, as in Lindau's hemangiomatosis. Hemangiomas elsewhere, in the face and scalp, may also link him with the plastic surgeon, who occasionally sees a large nevus in conjunction with hemiparesis, due to an intracranial duplication of the same lesion.

There are several conditions in which the neurological surgeon may work in conjunction with the otolaryngologist. Mucocoeles of the frontal sinus may have such great proliferation that they extend intracranially—even into the ventricle. Cerebrospinal fluid leaks from the nose must sometimes be repaired from the inside by a fascial transplant. Parotid tumors, etc., may make nerve anastomosis necessary because of destruction of the facial nerve. Cholesteatomas may extend intracranially from the external structure of the ear.

Finally, although it is probably beyond the scope of this group, the discovery of papilledema, optic atrophy, or visual field change may lead directly to the neurosurgeon. Conversely, the neurosurgeon's case of acromegaly may lead, in addition to the radiologist, to the dental surgeon.

In all, it may be seen that the services of the neurosurgeon have their occasional value to the group.



## DIVISION OF RADIOTHERAPY

The physician in charge of the division of radium and X-ray therapy should have modern shock-proof therapy equipment, carefully calibrated by the biophysicist. Radium in the form of plaques, tubes and special moulds should be available as well as removable platinum needles containing radium element and gold-filtered radon seeds. In addition to his knowledge of radiotherapeutic technique, the radiologist should be trained in the clinical phases of cancer. He must know the limitations of irradiation for each type of tumor, and he must be acquainted with the efficacy of tumor surgery so that he does not accept for treatment a patient who might be better benefited by surgery. It is important that he understand the pathology of tumors so that he can evaluate the radiosensitivity of the lesion and plan the dosage accordingly for each case. The radiotherapist working with the head and neck surgeon has a two-fold service: first, to give his opinion in consultation with the other specialists in the clinical diagnosis of the patient, and second, actually to carry out X-ray and radium treatment when these forms of therapy are selected.

When the patient is presented to the group, the radiologist takes part in the consultation. After examining the patient and the microscopic specimen, he gives his opinion as to the radiosensitivity of the lesion and the possibility of cure by either X-ray, radium or both. Sometimes he may recommend preoperative irradiation to render a technically inoperable case operable after a preliminary course of treatment. In certain instances he may recommend postoperative irradiation.

For therapeutic consideration, tumors may be divided into three classes: first, the type that will require only surgical treatment; second, the type that should be treated by X-ray or radium or both; and third, the type that may be treated by irradiation or surgery or by a combination of both methods.

For the cases that require a combination of both methods of treatment, the specialists in the group work together. Sometimes it is necessary for the surgeon to prepare the patient for irradiation. For example, in cancer of the antrum, a Caldwell-Luc operation is performed to provide drainage before deep roentgen therapy is started. The oral surgeon is called upon to correct poor oral hygiene or to remove infected teeth before radiation is given. The latter measure is extremely important to prevent the complication of radionecrosis. He also prepares special dental moulds for the radium

treatment of intra-oral lesions. On the other hand, the radiotherapist may help prepare a case for surgery by administering preoperative irradiation in order to render a borderline case operable.

With the radiotherapist and the surgeon working as a team in the management of head and neck tumors, it is hoped that the controversial problem of radiation versus surgical treatment may be solved. Until a sufficient number of cases has been collected for statistical evaluation, the chief consultant makes the decision when a difference of opinion arises. The end result is then critically viewed by the entire group. In studying the cause of therapeutic failures, it must be remembered that many cases appear for treatment in an advanced stage of the disease. Therefore, in evaluating end results, cases should be divided into early, moderately advanced and advanced stages, and estimations made for each stage.

Radiotherapeutic treatment should be carefully planned and carried out in a precise manner. Before patients receive X-ray or radium treatment, certain conditions must be satisfied. The general condition of the patient is studied to rule out the presence of distant metastases, particularly in the lungs and bones. The patient's fluid intake must be adequate because dehydrated patients are known to respond poorly to irradiation. Complete blood counts must be made and secondary anemias corrected. Irradiation in the presence of a leucopenia is always hazardous and when present must be treated before radiation therapy is started.

It may be necessary to begin treatment with external irradiation in the form of deep X-rays or radium bomb. After external irradiation has been carried to the limit of skin tolerance, supplementary interstitial radium in the form of removable platinum needles or radon seeds may be indicated. Each tumor case requires a total dose sufficient to eradicate the lesion, but this cancerocidal dose should not exceed repair limits of the normal tissues comprising the tumor-bed. Lead shields are used to protect the normal structures. This is especially important when treatment is given in the eye region.

During the course of radiation treatment, the patient is examined by the entire group at regular intervals. When a lesion fails to respond as originally expected, it may be wise to stop X-ray or radium treatment and carry on with surgery. This may be due to the fact that certain tumors which under the microscope appear radiosensitive actually prove to be relatively radioresistant. How-

ever, if the experience of the radiotherapist leads him to believe that such lesions can eventually be controlled, he should be given the opportunity to deliver what he considers to be an adequate dose.

Throughout the X-ray and radium treatment, the therapist avails himself of the advice of the physicist, especially regarding the estimation of dosage in air, on the skin and in the tumor-bearing area. Clinical research is carried on by these individuals, such as the work with special phantoms to ascertain the qualities of various radiation beams.

There are three educational directions in which the radiotherapist can bring his findings to bear: first, to his colleagues in the group and to the profession at large; second, to medical students; and third, to the laity. Statistical studies made at specific intervals following treatment reveal valuable clinical conclusions. In addition, prognostic aids are obtained through the study of radiation reaction in biopsy material. Photographs taken before, during and after treatment not only provide accurate permanent records of case progress but are especially useful for teaching purposes. Finally, there is the task of overcoming the layman's unreasoning fear of X-rays and radium. This is accomplished by emphasizing the fact that properly executed treatment destroys the disease without harming the host.

#### DIVISION OF PATHOLOGY

The pathologist in this team has certain functions which only he, with years of full-time experience in a specific field, can satisfactorily perform. These include: 1) examination of the patient by the pathologist, in order that he may have the facts through his own senses; 2) advice to the surgeon as to where to take the biopsy from, and how (choice of instrument or method), and 3) suggestions as to supplementary laboratory procedures which might be of additional aid in differential diagnosis; an example is the interpretation of the Wassermann test (positive in 20% of cases) as well as the heterophile antibody reaction (Paul-Bunnell test) in suspected infectious mononucleosis.

The pathologist should advise as to the dangers of biopsy, not in general terms, but specifically in the light of the probable lesion and its location. Probably no carcinoma is further activated by properly performed biopsy, and the value of accurate diagnosis by biopsy far outweighs the remote (and unproven) hazard of spread of any tumor.

The question of evaluating the possible advantages against the disadvantages of the rapid diagnosis methods—particularly the frozen section method—should primarily be the pathologist's responsibility. The type of tissue, the amount of tissue, and the probable type of the lesion are the chief factors influencing the decision for frozen section in any case. There are other factors, such as the necessity for immediate diagnosis, the skill of the pathologist, and whether treatment can later be altered without harm to the patient, which must be considered. In general, small biopsies should be prepared by the paraffin method only and not be subjected to the risks associated with the frozen section methods. Lymphoid tissue does not permit of satisfactory frozen section diagnosis. In all doubtful lesions, the pathologist should be given ample time for a leisurely study of the tissue. The risks of the frozen section method should be understood by all concerned. The point is that here again, although the decision for the handling of the tissue is primarily the responsibility of the pathologist, the knowledge of the patient possessed by others may and should influence the diagnostic procedure as applied to the biopsy tissue.

The pathologist should contribute from his experience an opinion as to the probable malignancy of a given lesion. Since Broders in 1920 began the studies of histologic grading of tumors, the inclusion of an expression of the probable malignancy of a tumor in the pathologist's report has become of greater therapeutic and prognostic value. While the histologic and biologic criteria of malignancy are sometimes at variance in a specific tumor, the best plan for treatment can be formulated only when all the factors are considered. Facts concerning the distribution and order of metastases, the probability of multiple, multicentric, or successive tumors, the statistical biography of various tumors, and such similar data are often kept more in mind by the tissue-pathologist whose work keeps him routinely in closer contact with tumors of various types.

It is the function of the pathologist to express an opinion as to the radioresistance of the tumor, based upon its histological appearance and known biological characteristics. Again, the two do not always parallel. The final plan, then, must be the combined judgment of several persons, following consideration of all the known factors of the individual case.

Biopsy is of value in ruling out malignant disease as well as in establishing its presence. If this rule is adopted in head and neck work, many needless radical procedures will be averted, just as in

general surgery the biopsy often saves the needless amputation of limbs, breasts and other organs.

And last, the pathologist is to assist in the evaluation of methods of treatment. No matter how objective any person may try to be, it is but human for each individual to see his successes more clearly than his failures. It is but natural that every man believes his way of doing a particular thing is, at least for him, the best way. The pathologist, so far as clinical procedures are concerned, is probably most free from fixed ideas concerning the merit of various methods of treatment. To him, the evaluation of the results obtained by radium, X-rays or surgical treatment can be most nearly objective.

The foregoing, then, are the principal functions of the pathologist in any modern tumor study group. He is not indispensable to the function of such a group, but he is as indispensable as any other portion of the team, if the best interests of the patient are to be served.

185 NO. WABASH.

### LXXXIII

## THE AMERICAN BOARD OF OTOLARYNGOLOGY

WILLIAM P. WHERRY, M.D.

### OMAHA

At the outset it is well to state that the factual data herein presented are in a large measure an effort to portray in words a sequential array of intangible forces, the slowly developing climax of which predicated the necessity for and as an end result, the creation of the national examining boards in the medical and surgical specialties. In other words what follows is not to be interpreted solely as a history of the American Board of Otolaryngology.

Medicine in the past 50 years has, it must be conceded, made more scientific and practical progress than had been noted in the previous 500 years. This stepping-up of usable knowledge naturally broadened the scope and horizon of the better practitioners of medicine to the end that groupings of those particularly qualified ensued. Better medicine was recorded.

Early in the transitional period, ophthalmology and otolaryngology became recognized as potential specialties. Generally speaking, the earlier group prospered. What more natural than that individuals less well-qualified should invade the group? There existed no force to judge these self-exploited members. There was none to say, "No," except a slow developing economic challenge, which challenge became obvious as special practice expectancies reached a measurable stage. Medicine has always heeded a challenge arising from a just criticism.

In 1910 a proposal was made to the American Ophthalmological Society that a committee be designated which would create ways and means of evaluating the knowledge of those who professed ability as ophthalmologists. The following year a similar proposition was presented to the Academy. Consequently, a joint committee was appointed for both ophthalmology and otolaryngology.

The ophthalmological section proceeded to work. In 1916 at the Memphis meeting of the Academy, after a heated discussion the original motion was changed, and two committees were named, one for ophthalmology, and one for otolaryngology. In 1917 the Ameri-

can Board of Ophthalmology was incorporated. The Committee for Otolaryngology continued to function satisfactorily as an examining committee for membership in the Academy.

In 1924 a group of representative otolaryngologists was organized and in 1925 the American Board of Otolaryngology was incorporated.

Most of the representative national societies in otolaryngology accepted the Board as an authorized body and a certificate from the Board became a requisite for membership.

From 1925 until 1932 the two then-existing Boards (ophthalmology and otolaryngology) met with considerable resistance from other medical groups. The principles of Board philosophy seemed at the cross-roads of acceptance in organized medicine. However, in 1935 the turning point was apparent and since that date not only the original policies and objectives have been accepted, but elaboration of policies is now assuming a tangible result.

It must be recognized that if academic sources were able to supply the demand of 167 well-trained otolaryngologists each year, then the Boards would resolve themselves into appraisal bodies of graduates, and through this appraisal simply rate graduate sources in otolaryngology.

Let it be pointed out, however, that at the present time though the higher standards of otolaryngological training are somewhat confused, yet the minimum requirements expected of good safe practitioners professing otolaryngology as a specialty are definitely defined. In this connection the economic demand for 167 new otolaryngologists each year is met with only about 70 from academic sources; the gap between 167 and 70 will be filled and it is for this group receiving their specialist's preparation working as assistants, in dispensaries, or those who through perseverance have picked up their preparation in any way possible that Board surveillance becomes advisable.

That the level of a good intelligence ratio has been decidedly raised in this group filling in the gap mentioned there can be no doubt. Likewise the influence of the Boards through appraisal of graduates of academic sources has had a wholesome effect upon those conducting graduate courses and residencies. In fact faculties now realize the necessity of delivering services to students. Perhaps it may be stated, as a subtle pat on the back, the Boards have made catalogue promises mean something.

One and perhaps the principle original objective of Board philosophy was to designate a diplomate as a man possessing a safe usable knowledge of the specialty concerned, and one to whom the public could safely appeal in time of need. In no sense does the possession of a certificate label the holder as a superman.

Let it be remembered that the personnel of an examining board are in no sense themselves supermen; they may be idealists, but they are nevertheless human and are chosen from among those who are willing to make the sacrifice, to serve, and to bring to the group simple, good, common sense and judgment backed by a broad-gauged viewpoint. Differences of opinion are desirable, yet there must be a willingness to mould an individual trend into a group conclusion. In other words, a Board of Examiners (appraisers may be a better term) teamed to group thinking can fulfill and build to the ideal objective. The contrariwise result may follow where a Board is dominated by a few or where a self-constituted clique assess themselves as supermen.

In reviewing 15 years of service, the panorama of events, the changes already affected in otolaryngological practices, in the academic structure of graduate education in otolaryngology—all these things accomplished should be looked upon as a sincere effort to heed the demand of economic necessities, to carry on the traditions of medicine usually to correct its own errors from within.

Let it be stated in closing that the objectives of the Board were conceived by those possessing a long-range vision of what should be. And it must be further realized that the objective in its entirety will need the continuance of this same long-range visualization, a maintenance of sound practices, good judgment, proper thinking.

The build-up of efficiency standards from the economic viewpoint of public service presupposes not only a high level of good safe medicine by those in practice, but also postulates a necessary surveillance of graduate medicine in the development of judgment planes in the formative period of an educational program.

1500 MEDICAL ARTS BLDG.



## PNEUMATIZATION OF THE PETROUS PYRAMID\*

J. R. LINDSAY, M.D.

CHICAGO

The anatomy of the human temporal bone, because of its complexity and many variations, does not lend itself to any simple method of demonstration.

The possible variations in the arrangement of the middle ear air cell system are a matter of great importance in suppurative disease for interpretation of the clinical picture, for X-ray demonstration and for surgical approach.

The location, frequency, developmental pathway, and method of X-ray demonstration of the possible extensions of the cell system into the petrous portion have been described in previous reports.<sup>1, 2, 3</sup> Examples of suppuration in each area have been demonstrated both of histopathology from fatal cases and X-rays and case reports of cured cases.

Serial microscopic sections of the temporal bones have proven to be the only accurate method of studying pneumatization of the pyramid, but for the purpose of demonstration they have the disadvantage of being difficult to interpret without considerable study. The reconstruction of models by the wax plate method is suitable for accurate anatomical study, but the models require much time to prepare, and do not particularly simplify the demonstration to the student.

For the purpose of simplifying and clarifying the anatomical arrangement of the various types of pneumatization a series of semi-diagrammatic illustrations have been prepared which the author has found to be most useful. The drawings as well as the percentage figures on pneumatization are based on the pneumatization studies previously reported.<sup>2</sup>

The routes by which cell tracts extend into the pyramid provide the key to the simplest clinical classification of petrositis, and

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\*From the Division of Otolaryngology, School of Medicine, University of Chicago.

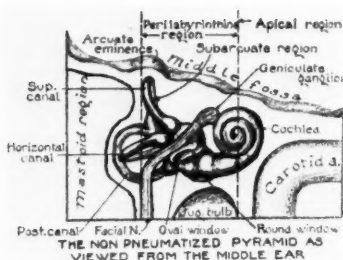


Fig. 1.

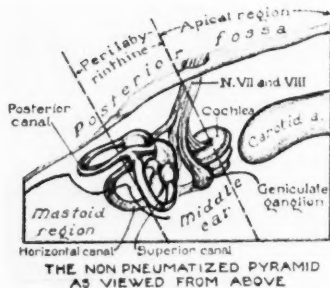


Fig. 2.

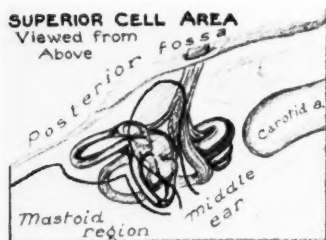


Fig. 3.

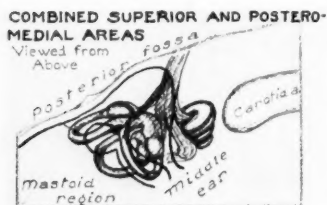


Fig. 4.

Fig. 1. The non-pneumatized pyramid as viewed from the middle ear.

Fig. 2. The non-pneumatized pyramid as viewed from above.

Fig. 3. Single cell tract from the epitympanum into the angle of the pyramid. 17%.

*X-ray projection required*—Stenver's or transorbital.

*Surgical approach:* 1. Elevation of dura over arcuate eminence. 2. Via aditus (feasible in limited number).

Fig. 4. Cell tracts from epitympanum, and from the mastoid by way of the angle. Tracts may remain discrete or unite. 17%. A third tract through the subarcuate region may exist. This tract was found to exist alone in 3%.

*X-ray projection required*—Stenver's and occipital views combined.

*Surgical approach:* 1. Intrapetrous, through the angle, from the mastoid. 2. Extrapetrous—over the arcuate eminence, if extradural abscess is present. 3. Via subarcuate fossa, if pneumatized tract present.

at the same time indicate the most feasible routes by which the surgical approaches may be made. The illustrations on pneumatization therefore constitute a convenient reference for clinical purposes and for the choice of surgical procedure.

Figures 1 and 2 indicate the division of the pyramid into mastoid, perilabyrinthine and apical portions. They show the non-pneumatized pyramid, the condition in two-thirds of all adults.

Figures 3 to 10 inclusive illustrate the common types of pneumatized pyramids. These fall into the simple classification shown in the chart.

The simplest clinical classification of petrous pyramid suppuration is the division into posterior and anterior petrositis, the former occurring in case of pneumatization by the posterior route, the latter in the case of the anterior route. Either type is likely to be associated with varying degrees of osteomyelitis.

In the author's experience the relative frequency has been: posterior petrositis, 70%, and anterior petrositis, 30%.

The possible surgical approaches in each type of case have been indicated in the legend beneath each illustration as well as the X-ray projection which is most suitable to demonstrate the area. In each case the surgical approach found to be most useful by the author is mentioned first.

These illustrations have been designed for help in orientation in the study of pneumatization of the temporal bone. They are based upon and correlated with previous reports on petrous pyramid anatomy and pathology.<sup>1, 2, 3</sup>

950 EAST 59TH ST.

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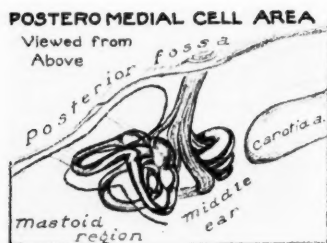


Fig. 5.

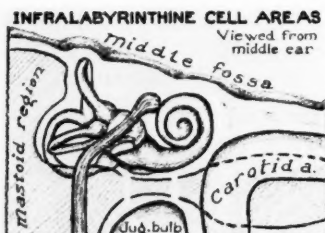


Fig. 6.

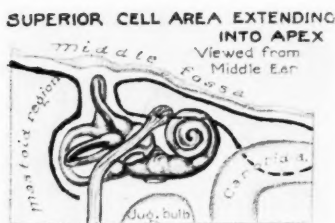


Fig. 7.

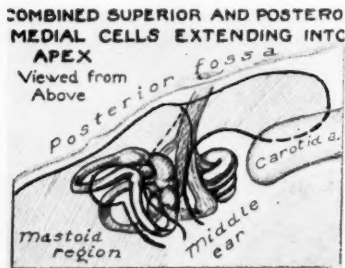


Fig. 8.

Fig. 5. Posteromedial cell area. Tract leading from mastoid into posteromedial cell area, between the posterior cranial fossa and endolymphatic aqueduct, but doesn't extend up into the angle. About 8%. (About 25% when type shown in Fig. 4 is included.)

X-ray projection—Occipital view.

Surgical approach: 1. Intrapetrosal—via the mastoid. 2. Extrapetrosal—by elevation of dura, when extradural abscess is present.

Fig. 6. Infralabyrinthine cells—25%. Details as to development and variations given in previous report.<sup>2</sup>

X-ray projection—No satisfactory method.

Surgical approach: 1. Retrofacial cells are reached from the mastoid. 2. In a very small percentage an approach to the apex is possible from the retrofacial cells. 3. From middle ear.

Fig. 7. Extension of superior perilabyrinthine cells into apex. (Usually an extension of type in Fig. 4.)

Fig. 8. Extension of perilabyrinthine cells into the apex. Viewed from above—7%.

X-ray projection—1. Stenver's. 2. Axial. 3. Transorbital.

Surgical approach: 1. Intrapetrosal—through the angle following simple mastoidectomy. 2. Intrapetrosal—through the subarcuate region when cell tract exists. 3. Extrapetrosal—by way of the middle fossa.

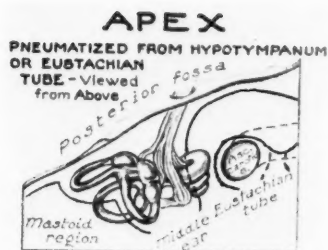


Fig. 9.



Nos. 1, 2 and 3 indicate areas from which pneumatization may extend into apex. Surgical Approach most feasible thru these areas.

Fig. 10.

TABLE I

## PNEUMATIZATION OF THE PETROUS PYRAMID

POSTERIOR ROUTE		ANTERIOR ROUTE
Perilabyrinthine	Apex	Apex
Superior cell area (only). (See Fig. 3.)	(Extension of perilabyrinthine cells)	From hypotympanum or eustachian tube mouth. (See Figs. 9 and 10.)
Superior and posteromedial cell areas combined. (See Fig. 4.)	Superior cell area extending into the apex. (Fig. 7.)	
Posteromedial cell area only. (See Fig. 5.)	Combined superior and posteromedial areas, extending into the apex. (Fig. 8.)	
Infralabyrinthine area. (See Fig. 6.)		

## THE ROLE OF NUTRITION IN INDUSTRIAL HYGIENE\*

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We very often fail to make the connection between the experimental and theoretical work in which so many hundreds of people are engaged in this country, and the practical, everyday medical and preventive medical problems that confront the profession. I can well remember when no respectable medical man would have anything to do with the word "vitamin" or consider that it had any place in medical practice. As a matter of fact, the present use of vitamins, their popularization, and the understanding of and interest in them by the medical profession is a matter of slow but recently cumulative growth. Progress has been fast in the last ten years and will be faster in the next ten years, undoubtedly.

I will briefly discuss four different things. First, I want to say a few words about the identity of the members of the vitamin B complex, because that is the most recent and perhaps the most interesting development in the nutrition field. Second, I wish to point out some of the symptoms resulting from deficiency of these B vitamins, the clinical symptoms that are recorded in the case histories in the journals, and the sub-clinical, rather vague symptoms and conditions which are not always tied up in our minds with the deficiencies which probably caused them. Then, third, I want to say a little about the chemical and histological changes that accompany these deficiencies, in so far as we know them, and lastly, a little about the application of these findings to industrial hygiene. By industrial hygiene, I refer to both preventive and curative processes.

### 1. *The Unravelling of the Vitamin B Complex*

All of you know, without being reminded, that this complex some 50 years ago was supposedly one thing and wasn't baptised vitamin B until 1914. It was thought to be only one thing, a beriberi-preventing substance, until 1919. I well remember the first article

\*Presented before the staff meeting of the Southern Pacific Hospital, San Francisco, May 14, 1941.

in the *Journal of Biological Chemistry* by H. H. Mitchell in which he pointed out, without any conclusive experimental basis, undoubtedly there were two parts to vitamin B. There was not any experimental proof of this until 1926, when Goldberger began his studies with both animals and humans, in the hope of discovering what deficiency caused the symptoms of pellagra. He produced certain symptoms of deficiency in rats by a diet which we know now was not pellagra-producing, but which was deficient or low in riboflavin. So I think we might say that riboflavin was the second of the B vitamins to be uncovered. But by 1928 suspicions of a third one were evident in the literature. The British workers Chick and Copping suggested this as "substance Y" about that time.

In 1933 Kuhn of Heidelberg published his findings on riboflavin and identified this as a vitamin. This was confused for a year or so with the PP factor which was supposed to be the pellagra-preventing factor of Goldberger.

So, the first vitamin to be chemically unravelled was riboflavin and this work was done by Kuhn of Heidelberg. It is rather interesting to note how active the German chemists have been, beginning in the early thirties, in trying to determine the exact chemical structure of these vitamins and also to find means of synthesizing them. This work, I suspect, can be assigned to war preparation. It was all part of the plan. Undoubtedly the German physicians and German nutrition workers, of whom Richard Kuhn is one of the outstanding members, knew that in case of blockade, Germany would not be able to obtain natural foods in sufficient amounts to provide these rather vague substances which they already recognized as important for both physical and mental health, and so they wished to know the structure of these substances so that they might be made in the laboratory.

The next substance to be suspected as of separate character was that which Paul Gyorgy, working in Kuhn's laboratory, called vitamin B<sub>6</sub>. We had B<sub>1</sub> to start with, thiamin or the anti-beriberi factor, then riboflavin called B<sub>2</sub>, before its structure was known. In the meantime in 1934 and 1935 unknowns called B<sub>3</sub>, B<sub>4</sub> and B<sub>5</sub> had been postulated by various workers, so vitamin B<sub>6</sub> was next in line and Gyorgy called this substance, the third member of the B complex, B<sub>6</sub>. This, too, has been identified, its chemical character uncovered this time by Americans rather than by the Germans, and it is now called pyridoxin. It is a pyridine derivative, the first such compound found to have vitamin characteristics. Thus there were three B vitamins by 1935.

But in 1936 a group at Wisconsin and another group in California discovered that there were at least four substances in the vitamin B complex, and this fourth one has been generally called the filtrate factor or factors, simply because the other three previously identified adhere to Fuller's earth and other colloid holding substances, so that when a concentrate is shaken up with Fuller's earth, these three vitamins adhere and the filtrate separated from that earth contains something else. The filtrate factor this was called at first, but it should be in the plural because there is certainly more than one. In the meantime, by a series of two cases, nicotinic acid had been suggested as possibly the antipellagra substance. The Wisconsin group again made this study and found that dogs with black tongue, which is supposed to be the analogue of pellagra, if given doses of nicotinic acid, appeared to have the symptoms cleared up almost immediately. Almost at once this was tried on pellagrins and immediate relief of some of the most striking symptoms was noted, so that nicotinic acid and nicotinic amide, both of which are active, have joined the group of B's, making the fifth of the group to be identified. Nicotinic acid is a very simple, cheap substance, the chemical character of which has been known for at least 50 years, and it has been, of course, synthesized.

The filtrate fraction was worked upon in very many laboratories, very actively by our own chemists and in Wisconsin and particularly in Roger Williams' laboratory, where the existence of certain yeast and bacterial growth-promoting substances had long been studied. Somebody suspected that at least one of the filtrate factors was identical with the pantothenic acid which Williams had shown to be active for yeast, and there is a very interesting story of ingenious experiments and guesses involved in the clues that were obtained as to the structure of pantothenic acid. It had been found by Williams that asparagine, which contains beta amine group, would promote the growth of yeast which had been deprived of this pantothenic acid. He then tried beta alanine, a similar compound, because it was available. It was also effective, and from then on the rest of the molecule was hunted down until in Merck's laboratory early in 1940, the actual structure of pantothenic acid was worked out and its synthesis perfected. Drs. Jukes and Babcock of Davis have also synthesized pantothenic acid in a somewhat different way.

That is the story of the group so far. Now in the last year since pantothenic acid was nailed down, it became possible to feed animals with crystalline products representing these five substances, thiamin, riboflavin, pyridoxin, the filtrate factors including panto-





Fig. 1. Terminal condition of rat deficient in the filtrate fraction of the vitamin B complex for two years. Note greying fur and loss of fur, swollen legs, extruded testis.

thenic acid. It is very interesting to notice what happens. Is this all? Do we know all, or is there still something else to be added? There are evidences that there are still some gaps in the vitamin B complex. One of these appears to be choline. This is now called one of the vitamin B complex, although I think there might be some question as to whether it should be called a vitamin. In the first place it is required in rather large amounts for a vitamin, and I think it is not altogether clear as yet that it is actually required by more than one or two species. However, let us include choline. Biotin is another substance which has been identified as being similar to or identical with the anti-eggwhite injury factor and perhaps coenzyme R, a bacterial growth-stimulating substance which has been known for some five or six years. Biotin may be added although its chemical structure is unknown. Para-amino-benzoic acid has been suggested also as part of the complex necessary for the darkening of the fur and the repigmentation of the animals which have been greyed by deficiency of the filtrate factors.

## 2. *The Deficiency Symptoms*

This greying effect was the first small contribution from our laboratory on the subject of the filtrate factors. We found in 1936 that rats that received the three first recognized B vitamins, thiamin, riboflavin and pyridoxin, grew rather poorly, showing progressive

symptoms of senility, the most striking of which was the greying of the fur. We noticed this because we used black rats, and we saw this stippling of the fur if the animal were kept on the deficiency long enough. The fur became completely grey and the animal showed very striking senescence. When I described this finding at the Memphis meeting of the American Institute of Nutrition there was quite a good deal of polite chuckling in the corridors even by some of my colleagues who really knew more about it than I did—but it has turned out that it is probably a universal symptom of the deficiency. We have seen it in our laboratories not only in rats, but in dogs, silver foxes, guinea pigs, and chickens and recently in the wild blackbird, so that it would appear to be a universal trait. The greying of the hair, possibly even in humans, is certainly promoted by the deficiency, but this is the least important of the symptoms that are found. We found that the adrenal gland, particularly the cortex or rather the margin of the cortex next to the medulla, the reticularis line, was badly damaged in cases of this deficiency and, perhaps as a sequence of this damage, rather striking damage was seen in other glands, particularly in the thyroid and in the sex glands. The skin becomes dry and wrinkled, and according to Dr. Jesse Carr, it loses its elastic layer completely and is like an extremely senescent skin. On readministering the thing that we are still calling the filtrate factor, all of these changes reversed themselves, repigmentation of the fur began almost at once and repair of the glands took place. These are the symptoms of the deficiency, the second point that I wish to mention.

### 3. *The Tissue Changes in Deficiencies*

Apparently the filtrate factor deficiency, which is probably largely, but not wholly, pantothenic acid deficiency, has a rather definite tie-up with the endocrine system. Whether the adrenal cortex is first affected by the deficiency, or whether something else, possibly the anterior pituitary, is first affected and the adrenal cortex is next acted on and then the thyroid and sex glands, and others further affected through the mediation of the adrenal, cannot be definitely stated at this time. But the damage to the adrenal cortex has been abundantly confirmed in a number of laboratories. A new observation, however, seen in our laboratory in animals that received nicotinic acid but did not receive the filtrate factor, is that the type of adrenal damage is quite different from that in the animals that did not receive either nicotinic acid or filtrate factor. The cortex is damaged in both cases, but there are hemorrhages into the medulla also in the animals that received the nicotinic acid. We found some



Fig. 2. Black cocker spaniel, two years old, reared from weaning on a purified diet plus only thiamin, riboflavin and pyridoxin of the B complex. Note greying of fur.

time ago that in these grey rats we can produce the same syndrome by giving them excess nicotinic acid or injecting adrenalin. I believe we have here the first inkling of the damage done by imbalance of these vitamins.

#### 4. *Nutrition in Industrial Hygiene*

Now to get to the last point, the bearing of these things on practical industrial hygiene. In the first place, possibly these elderly looking rats and dogs which were really not elderly at all, may have reminded you of some people that you know. I think of some who are young in years but who have all the symptoms of premature senescence: greying hair, dry and wrinkled skin, lack of appetite, nervousness, insomnia, gastro-intestinal difficulties. I don't know what the order is in which these occur, but they do occur. We made a number of fractional gastric analyses in the filtrate-factor-deficient dogs and found no hydrochloric acid produced at all. Even with histamine we could not get any free acid, whereas in the dogs with the filtrate factor we had a normal response. In these deficient animals also the stomach action was extremely slow. Twenty-four hours after they were fed we found food residue in the stomach, but

none in the normal controls. Similar difficulties occur in humans, apparently without any reason, what you medical people call organic or degenerative disease. Why do middle-aged people have the troubles they have? Why do these inevitable aging symptoms appear? Of course they happen sooner or later in everyone. But perhaps they are not inevitable before a good many years later than the three score and ten we are warned about, even though these symptoms of premature aging are characteristic of our modern urban civilization and particularly of our high-powered executives and leaders. There are seen even in people whom, by other appearances, one might expect to be fairly young, surely not beyond the thirties, grey hair and other little tell-tale symptoms that go with it, indicating that the deficiency is operating elsewhere than on the scalp.

Suppose that there occurs long-continued but only slight deficiency in these various factors, not only in the filtrate factors but in all the necessary vitamins, and that this eventually produces the premature aging. Suppose that we are all subjected to such slight deficiency all our lives, beginning with the infants artificially fed because their mothers can't nurse them as a result of dietary deficiencies and continuing with ordinary unfortified cow's milk, which is low in many of these factors, as their main food, with fruits and vegetables which are variable in vitamin content, as well as meat and processed grains.

A survey of the actual vitamin value of foods produced in this state, on different soils and under different climatic conditions, and different varieties of these foods would be well worth while. For instance, of green peas grown in California some varieties have 8 mg. of ascorbic acid per 100 gms. and other varieties have up to 33 mgs. per 100 gms. Almost the same range can be found in strawberries, and apples can vary greatly. We think of oranges, lemons and grapefruit as citrus fruit of similar qualities, but there is a great difference in their carotene content, lemons and grapefruit being without this provitamin A while oranges have measurable amounts.

With all the knowledge of nutrition that is available now, how much do you advise your patients in regard to diet? Most medical men who advise their patients in regard to diet usually tell them to eat a good, well-balanced diet, to take plenty of milk, fruit and vegetables. But a diet of milk, fruits, and vegetables can readily be a low vitamin B containing diet, depending upon what fruits and vegetables are included and even what variety of the fruits and vegetables are used. To be sure, if the volume of food eaten is great enough the danger of deficiency is relatively less, but in our day total



Fig. 3. Cocker spaniel reared on purified diet plus thiamin, riboflavin, pyridoxin and pantothenic acid, but without nicotinic acid. Note complete paralysis. Similar conditions were present in other dogs fed the same diet plus thiamin, riboflavin, pyridoxin and nicotinic acid but without pantothenic acid or filtrate factor.

food intakes are no longer large. I imagine that few people eat more than 2500 or 3000 calories a day, and without extreme care in the choice of the foods with, say, 2500 calories, it is difficult to get the amount of vitamins actually needed, to say nothing of an excess of these vitamins. I have tried to figure out for my own benefit a diet containing 1800 calories providing sufficient vitamins as well as variety and edibility, and I find it very difficult, even making the selection with the help of the information available in the most recent tables of food values.

Vitamin deficiency, especially vitamin B deficiency, I believe, is rather widespread and if we judge by what happens to animals in our laboratory, many of the things that are happening to humans producing illness and breakdowns, lost time and early old age, may be due to these rather complicated, long-continued, perhaps only slight, deficiencies. Vague symptoms that are never recognized as frank dietary deficiency diseases may nevertheless be ascribable to partial nutritional deficiency. So, I should recommend to any industrial group attempting to improve the efficiency of the personnel,

to consider very seriously what can be done to find out whether nutritional deficiency exists among the personnel and particularly among the executives and the key men, the prolonging of whose life and efficiency is greatly to be desired. Those people should be examined, any deficiency symptoms recognized and such deficiency corrected. Of course, miracles will not result, but some remarkable improvement has been seen in a number of cases that have been handled in this way.

Finally, in the matter of defense and nutrition, I can't help but say a word about morale. That is an overworked word, and yet it is one that we will have to deal with in the next few months or years. The prepellagrins show a psychological condition of fear, nervousness, worry, and lack of courage as the very first detectable symptoms; before any physical symptoms present themselves, this prepellagrous change in personality takes place. We don't want any prepellagrins in this country. It can be prevented, but it is a huge task. It can be prevented in the armies, and the European armies have already shown what can be done. I have recently seen an article describing the Germans' war ration, which has fortified bread containing synthetic vitamin B<sub>1</sub>, soy bean powder and various fruit and vegetable powders which are stabilized so that the vitamins are protected in some way that is not altogether clear to us.

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## INFECTIONS OF THE MASTICATOR SPACE\*

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LOS ANGELES

From the title of this paper one might assume this to be just another addition to the already confusing array of spaces described in the head and neck by both the anatomist and the surgeon. Such an assumption would be quite natural. However, let us remember that these spaces are described because of their pathological significance and not because of their apparent anatomical ambiguity.

Any region which by virtue of its anatomical position, relations and conformity is consistently the seat of a pathological process causing characteristic clinical symptoms, is deserving of recognition. The masticator space is such a region. Abscesses in this space are usually dental in origin, give a characteristic clinical picture and tend to remain within certain definite anatomical confines. Because the signs and symptoms so simulate pharyngomaxillary disease, these cases are frequently seen by the laryngologist.

Our attention was first attracted to this region by cases diagnosed as pharyngomaxillary abscess of dental origin. We found, however, at surgery that pus was recovered not from the pharyngomaxillary space but from beneath the periosteum of the mandible. After changing our diagnosis to subperiosteal abscess of the mandible, we discovered that we were dealing with disease of the masticator space described by Collier and Yglesias<sup>1</sup> in 1935 and elaborated upon clinically by Dingman<sup>2</sup> in 1939.

The masticator space may be described as a fascial sling containing the muscles of mastication and the ramus of the mandible (Figs 1, 2, 3, 4). In its posterior portion it is bounded laterally by

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Presented before the Western Section of the American Laryngological, Rhinological and Otolological Society, San Francisco, California, February 2, 1941.

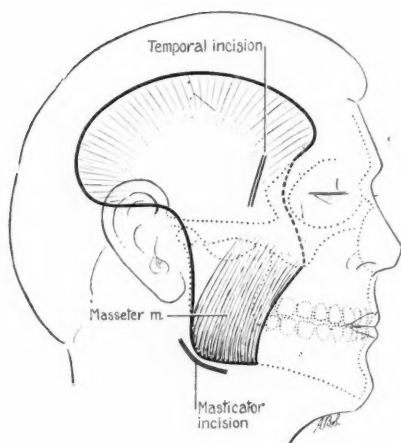


Fig. 1. Lateral view showing extent of the masticator space (Coller and Yglesias). Heavy lines indicate the boundaries of the space. The region containing the lower teeth and lying anterior to the masticator muscles is the space for the body of the mandible (Coller and Yglesias). The temporal and masticator incisions are shown.

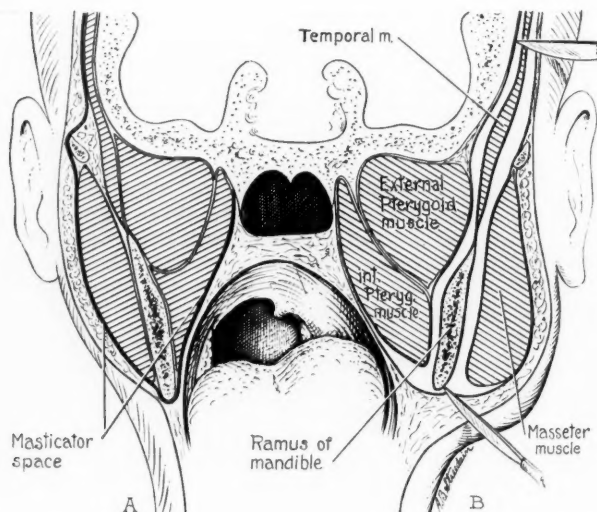


Fig. 2. Diagrammatic frontal section. Heavy lines represent the fascial sling, containing the masticatory muscles and the ramus. A—Normal side. Fascia is attached to mandibular periosteum inferiorly. The periosteum is firmly adherent to the mandible along its inferior aspect. B—Diseased side. Intra-oral and external swellings both are shown. Extension upward along the ramus into the temporal pouches is clearly seen. Scalpels indicate the extent of the masticator and of the temporal incisions.



the parotid gland, while its medial neighbor is the pharyngomaxillary region (Fig. 3). This fascial sling is, in reality, the fascial covering of the masticatory muscles which is attached to, and reinforces the mandibular periosteum inferiorly (Fig. 2A). The dissections of Coller and Yglesias have shown that it is a continuation of the cervical fascia which, anterior to the masticator space, helps to form the space for the body of the mandible (Figs. 1-3). Because the two spaces are continuous subperiosteally, and because of the firm attachment of the periosteum to the inferior surface of the mandible, infection easily passes posteriorly from the molar region into the masticator space (Figs. 3-4). The strong periosteal attachment inferiorly also forms a firm barrier against extension into the neck. Infection, having reached the masticator space, may proceed superiorly along the ramus to enter the temporal area. This area is divided by the temporal muscle into a deep and a superficial pouch. Pus burrowing along the medial aspect of the ramus enters the deep pouch, while extension along the lateral aspect leads to the superficial pouch (Fig. 2B).

The masticator space is most commonly invaded from the lower molar region. In some cases the sublingual and pharyngeal swelling predominates while in others the most prominent swelling is external along the ramus and the jaw angle. It is our feeling that in the former group the disease has extended along the medial border of the mandible toward the internal pterygoid, and in the latter group the masseter muscle has been reached along the lateral border of the mandible (Figs. 2-3-4). In both groups, the outstanding and common symptom is trismus.

The well-known phlegmonous swelling of the jaw resulting from external trauma, dento-alveolar disease or dental extraction which subsides within a few days without suppuration, is due to an inflammatory reaction of the contents of the masticator space. However, in this report we are dealing only with cases of abscess.

All cases have had trismus, fever (sometimes with chills), dysphagia, and signs of toxic absorption. There has been brawny induration over the ramus and the angle, or there has been sublingual and pharyngeal swelling. In most instances the internal and the external signs have coexisted. In only one case was there an absence of any external swelling. Tenderness along the ramus and in the subangular space has been constant, and the subangular space at the jaw has always been at least partially obliterated to palpation. Thus the signs and the symptoms may be indistinguishable from those of pharyngomaxillary abscess.

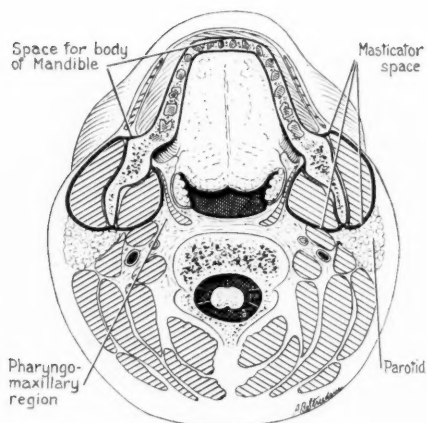


Fig. 3. Diagrammatic cross section. The heavy lines bound the masticator space. The space for the body of the mandible is shown as being continuous subperiosteally with the masticator space. Note that the internal pterygoid which is the medial boundary of the pharyngomaxillary space is contained within the masticator space. The pharyngomaxillary and masticator spaces are not connected. The parotid lies outside the masticator space. It is easily seen how medial extension causes intra-oral signs and lateral extension causes external signs.

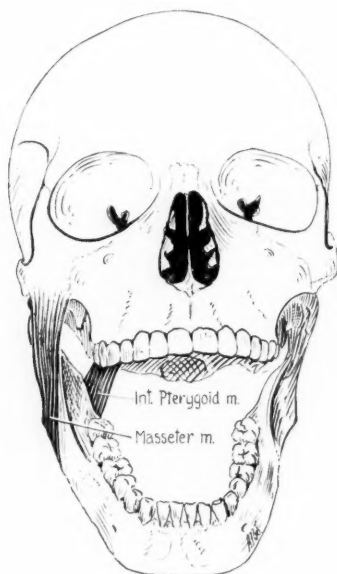


Fig. 4. Diagram showing the lower portion of the musculofascial sling formed by the masseter and the internal pterygoid muscles. Anterior to these muscles is the body of the mandible containing the teeth.

Twenty consecutive cases, seen in clinic and private practice, presenting the above signs and symptoms gave a definite dental history.

The typical history is that of a molar extraction or trauma to the mandible followed by trismus, swelling and pain, within a few hours. Frequently these signs have appeared almost immediately. However, instead of remaining at a standstill and subsiding in a few days as in the contusion cases, this type has shown a rapidly increasing process reaching its peak in three to seven days. These signs and symptoms then remain or become more marked until drainage occurs or becomes necessary. Only two cases in our group presented a history at variance with the above (Case 6 and Case 20).

Of the 20 consecutive cases of masticator abscess, 18 followed dental extraction alone, one followed fracture into the socket of a diseased third molar and one followed molar extraction plus external trauma to the mandible. The third molar was involved in 14, the second molar alone in two, and the first molar alone in three cases. In only one case was a premolar the only tooth extracted. Thus, the primary source was molar in 19 of the 20 cases.

In nine cases there was spontaneous intra-oral drainage. This occurred from the fourth to the eighth day, and in each instance resulted in prompt subsidence of symptoms and an uneventful recovery. The point of spontaneous drainage was consistently from the lingual border of the mandible near the base of the tongue. We noted in this group that the intra-oral signs predominated, and that dysphagia was a prominent symptom. Sublingual involvement prevented satisfactory depression of the posterior portion of the tongue, and there was usually some peritonsillar swelling present. Indeed, this type of case has been considered by some to be Ludwig's angina. However, if the term "Ludwig's" is to be used at all, we prefer to restrict it to cases of massive involvement of the floor of the mouth.

In only one case was internal incision and drainage required or deemed advisable. Two weeks following an uneventful right third molar extraction, the patient fell and struck her right mandible in the masticator region. Rapidly increasing trismus resulted. One week after the fall she consulted us, and at this time there was intense trismus and the tenderness over the ramus was very marked. No external or internal swelling was present at this time. A radiograph of the mandible disclosed no bony pathology or fracture. Two weeks following the fall, pain in the ear became excruciating, dysphagia was increasing rapidly and the trismus was so intense that the



Fig. 5. Photograph of Case 10. Right masticator space abscess which drained internally on the fourth day. Intra-oral swelling predominated. Note the trismus.

incisors could be opened only to the extent of about  $\frac{1}{2}$  cm. Examination at this time revealed a large pharyngeal swelling simulating peritonsillar abscess. This latter diagnosis was easily ruled out, however, because of the absence of tonsils and the fact that there had been no preceding pharyngitis. Internal incision was done with some difficulty because of the trismus, and it resulted in the discharge of a large amount of foul pus under pressure. The trismus rapidly decreased, the discharge continued for one week, and the patient was entirely well ten days following the incision.

In ten cases, external drainage was required. In six of these, the surgical drainage was performed within ten days of the onset of the masticator symptoms, and in all but one, an uneventful recovery resulted. The one case which drained for three months with sequestration was one in which a premolar had been extracted 12 days before the masticator symptoms. The history of this case suggests that an osteomyelitis of the body of the mandible was progressing before invasion of the masticator space became manifest.

In four cases masticator signs and symptoms had been present for two weeks or more before drainage was instituted. It is worthy of note that all of these patients are still draining after several months and all have developed osteomyelitis.



Fig. 6. Photograph of Case 12. Left masticator space abscess requiring external incision on the ninth day. Note the marked swelling and the extreme trismus.

It seems very significant that two patients had curettage of the tooth socket following extraction, and each has had a very stormy course. One developed a diffuse osteomyelitis necessitating the removal of all of the mandibular teeth. In the other, there was extension into both temporal pouches, an osteomyelitis of the ramus, a pharyngomaxillary abscess, and a deep perijugular abscess in the neck. Both patients are at present progressing slowly but satisfactorily.

In the treatment of these cases we have employed heat and chemotherapy during the first week. General supportive measures and parenteral nourishment have occasionally been necessary. No startling results have followed chemotherapy where a suppurative process has been present. Continuous hot compresses have been used externally, and where the trismus allowed, intra-oral irrigations have been employed. The latter have been universally unsuccessful in creating intra-oral pointing.

We agree with Dingman that unless the signs and symptoms become alarming, a week should be allowed before external incision.

From the results of these 20 consecutive cases, we believe that if spontaneous drainage has not occurred within ten days, and if the

process is unabated, external excision and drainage should be performed. In all cases late drainage has resulted in osteomyelitis and a prolonged unpleasant convalescence, while all molar abscesses which drained spontaneously or were incised surgically within ten days, terminated in an uneventful recovery.

The procedure of external drainage of a masticator abscess is important. The incision and drainage should be made just below and parallel to the angle of the jaw (Figs. 1-2B). The exact line for incision may be difficult to determine because of the extensive induration. Normally, only a few millimeters separate the skin and the angle of the mandible, while in abscess cases we have encountered a subcutaneous swelling and thickness of several centimeters. One must then cut and dissect through this tissue until the incision is carried to the bone (Fig. 2B). The fact that we have invariably had to carry our incision to the bone before recovering pus has led us to consider the process as being subperiosteal. Through this incision at the mandibular angle, one may explore the medial as well as the lateral aspect of the ramus (Fig. 2B).

If the temporal region is invaded it may be drained through a suprazygomatic incision (Figs. 1-2B). Both pouches may be drained through this incision, and if necessary, through and through drains may connect the temporal pouches with the masticator incision at the jaw angle.

So far in our experience, internal incision alone has not been satisfactory except where the intra-oral pointing was unassociated with the external swelling such as in Case 20 described above.

It must be remembered that alarming and dangerous symptoms may result from extensive involvement of the floor of the mouth. This area should be constantly observed and promptly drained when such symptoms present themselves.

#### CONCLUSIONS

From a review of 20 consecutive cases of masticator abscess, the following points should be emphasized:

1. Masticator abscess most commonly follows lower molar extraction.
2. The operative findings suggest that the pus is subperiosteal.
3. When pus is not recovered superficially, the incision must be carried to the bone.

4. The most destructive and extensive cases have followed curettage of the tooth socket.

5. Delay in instituting drainage has resulted in osteomyelitis and a strenuous convalescence.

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TABLE I

## 20 CONSECUTIVE CASES OF MASTICATOR SPACE ABSCESS

(Lower teeth were involved in all cases)

- 17 followed molar extraction
  - 3rd molar in 12 cases
  - 2nd molar alone in 2 cases
  - 1st molar alone in 3 cases
- 1 followed fracture into socket of infected third molar
- 1 followed third molar extraction plus external trauma
- 1 followed premolar extraction alone
- 9 cases drained spontaneously intraorally
- 10 cases required external drainage
- 1 case required internal drainage alone

TABLE II

## 9 CASES OF SPONTANEOUS INTRAORAL DRAINAGE

Case Number	Day of Drainage After Onset of Symptoms	Duration of Drainage	Tooth Extracted
18	4th	4 Days	Left Third Molar
4	7th	5 Days	Left Third Molar
11	8th	5 Days	Right Second Molar
10	4th	7 Days	Right Third Molar
8	6th	8 Days	Left First Molar
2	6th	5 Days	Right Third Molar
3	6th	4 Days	Right Third Molar
9	3rd	7 Days	Right First Molar
7	4th	4 Days	Left Third Molar

## 1 CASE REQUIRING INTRAORAL INCISION AND DRAINAGE

Case Number	Day of Incision and Drainage	Duration of Drainage	Tooth Extracted	Comment
20	14th after trismus 4th after internal swelling	7 days	Right third molar	Patient fell on right jaw two weeks after extraction.



TABLE III  
10 CASES REQUIRING EXTERNAL INCISION AND DRAINAGE

CASE NUMBER	DAY OF INCISION AND DRAINAGE	DURATION OF DRAINAGE	TOOTH EXTRACTED	COMMENT
19	10th	3 weeks	Right third molar	Uneventful recovery
12	9th	17 days	Left third molar	Uneventful recovery
13	5th	15 days	Left third molar	Uneventful recovery
14	2nd	2 days	Right second and third molars	Uneventful recovery
5	4th	4 weeks	Left third molar	Fracture into socket of infected molar
6	3rd	3 months	Left premolar	Extraction 12 days before masticator symptoms. Osteomyelitis. <i>Staph. Albus</i> .
1	6 weeks	3 mo. plus	Right first, second and third molars	Osteomyelitis
17	16th	3 mo. plus	Right third molar	Socket curetted. Osteomyelitis of ramus. Pharyngomaxillary, perijugular, and temporal pouch abscess. <i>Staph. Aureus</i> .
15	20th	4 mo. plus	Left first molar	Osteomyelitis. <i>Staph. Aureus</i> .
16	32nd	2 mo. plus	Left second molar	Socket curetted. Osteomyelitis, requiring removal of all teeth. <i>Strept. viridans</i> , <i>Staph. Aureus</i> .

LXXXVII

OTOLARYNGOLOGY FROM THE IMMUNOLOGIC  
VIEWPOINT

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From the time of Sydenham in the 17th century to the present day an unremitting quest for specific drugs to cure diseases has occupied the attention of medical men, and yet this endless search has brought forth but a meager list of drugs specific for an exceedingly small number of diseases. By the end of the 17th century the current of medical thought, diverted by the applications of the discoveries of Leeuwenhoek (1683) led men like Otto Frederick Muller of Copenhagen (1786), who named the bacillus, the vibrio, the spirillum, and Spallanzani (1729) to speculate upon infection of tissue by micro-organisms. This laid the groundwork of thought for the discoveries of Pasteur who toward the end of his career declared with prophetic insight that the physician of the future would be an immunologist. The focus of attention then deviated from the search for specific drugs to the matter of producing active immunity to disease. About 1880 Pasteur laid down the basic principles of that which is embraced in the concept of active immunization.

In the modern period of Robert Koch, Edwin Klebs, Metchnikoff and others the reaction of tissues to micro-organisms engrossed the attention of physicians, and the science of immunology assumed a position of capital importance in medical thought and practice. It is interesting to note that while this surge of immunologic study and investigation was reaching its apogee, the ancient urge to find the specific drug for a specific disease again emerged in Erlich's (1834-1915) search for an ideal *therapia sterilisans* in syphilis ending in the discovery of dioxydiaminoarsenobenzol. It is also interesting to note that in an age of swift progress in the development of specific sera, lysates, bacterial filtrates and vaccines there have appeared with dramatic suddenness sulfanilamide, sulfapyridine, and sulfathiazole, specific chemicals for the treatment of streptococcic, pneumococcic, and staphylococcic infections.

These three drugs because of the remarkable therapeutic results obtained in some cases have excited an unprecedented interest not only on the part of medical men but also of the laity.

It is well to pause, therefore, to inquire whether Pasteur's dictum that the physician of the future would be an immunologist was falsely prophetic, and whether it is more probable that the physician of the future will be a chemotherapist. It is difficult to observe the clinical effects of these new drugs critically, without the bias of undue enthusiasm. It may help to appraise them at their true value by remembering that mercury and the iodides are still of prime importance in the treatment of syphilis, despite salvarsan, that we know very little of the management of an acute suppurative sinusitis or an acute suppurative mastoiditis of the thrombophlebitic type by administering sulfanilamide. In other words future study and experience may limit the clinical use and value of these chemicals. The probability of this assumption is supported by much past experience in the history of medicine. The limitation of space for this article precludes enlargement upon this matter.

The purpose of this paper is to point with emphasis to the proposition that the field of otolaryngology is a field *par excellence* for the clinical study of immune processes. This is true for many reasons. Among the more important ones are:

1. The directly visible structures undergoing reaction between micro-organism and tissue (turbinates, septum and pharynx).
2. The great number and variety of infectious diseases originating in the otolaryngologic field.
3. The accessibility of structures for observation and manipulation.
4. The variety of tissues easily available for study, i.e., bone, other connective tissues, glands, lymphoid tissues and mucous membranes.
5. The facility of obtaining material for bacterial culture.

It is undoubtedly true that a greater number of otolaryngologists ignore immunologic therapy than employ it. For example, vaccine therapy in general is regarded as an uncertain procedure, of doubtful value, as something to be tried without great expectations. The writer hopes that he will not be held presumptuous in saying that vaccines are all too often used ineptly. Vaccine therapy is too frequently employed without knowledge of the basic facts of

immunology. Vaccine injections are given too often by the "rule of thumb". Vaccines are given with utter disregard of indications and contraindications. The slipshod use of vaccines is but a single example of the disregard of many clinical otolaryngologists for immunology. The writer does not intend that this paper should constitute a plea for vaccine therapy. The intention is broader in scope. No tissue which is involved in a reaction between itself and a bacterial invader can return to normal unless two, or one of two, events take place, namely, that the immunity of the tissue rise sufficiently, or else that the invading organism suffer attenuation (or loss of virulence). Moreover, it must be remembered that the human organism possesses a mechanism of defense which is constantly active to a greater or lesser degree. There are means or methods available by which these normal cellular and humoral mechanisms may be influenced or manipulated. Let us summarize briefly first what these mechanisms are, and secondly the means and methods which are known and are at our disposal to effect some measure of control and influence over them.

In the first place the blood and other body tissues which contain an appreciable amount of fluid substance contain varying amounts of antibody. Antibodies have the property of 1) clumping bacteria (agglutinin) hindering thereby their dispersion through hitherto uninvaded tissue; 2) dissolving bacteria (lysins); 3) enhancing their ingestibility by phagocytes (opsonins), and 4) neutralizing the toxic factors of bacteria (antitoxins). These constitute the humoral factors in immunity.

In the second place, but of equal, if not greater, importance, are the cellular factors. These cells wherever they occur conform to a definite pattern despite the fact that their morphology differs. 1.) They have a relatively large amount of cytoplasm and a relatively small nucleus. 2.) They are optionally fixed and stationary within a tissue, or they migrate. 3.) When migrating they assume the qualities and some of the characteristics of primitive unicellular, independent organisms, i.e., they travel under their own power (ameboid movement); they have the capacity to ingest particulate matter (bacteria for example), subject the bacteria to digestion, throw off a kind of excretion which is in reality specific antibody (there is abundant experimental evidence to support this statement); and they depart from the scene when no further bacteria remain, or they continue on the scene to take part in the repair of the invaded tissue by changing into fibroblasts. They are capable of exhibiting all of the phenomena of phagocytosis. There is an involved termi-

nology designating cells of this kind. In the liver they bear the name of Kupffer, in the spleen they are littoral cells, in the vicinity of blood vessels they are called pericytes, in the walls of the alveoli of the lung they are called dust cells, and in the omentum, clasmaticocytes. As a whole group they have been labeled reticulo-endothelial cells, histiocytes, fixed-wandering cells, polyblasts of inflammation, or simply macrophages. Whatever the general designation it is well to remember that regardless of their site of origin or their special morphology at any given moment, they all conform to the pattern described above, and they are phagocytic cells or they are potentially so. If one accepts the view of Maximow and others the term reticulo-endothelial is unfortunate in that these cells are not necessarily reticular cells, and are never of endothelial origin. They are found in varying numbers in all of the soft tissues of the ear, the nose, and the throat. Fenton has found that they increase in number within the sinus mucosa upon irritation of the mucosa, upon the injection of various substances into a sinus. The increase in their numbers, and their mobilization may be influenced by the injection of, or the surface application of, antigenic substances.

In general it may be said that it is possible to increase the amount of antibody in local tissues and to increase the number of phagocytic cells in the tissues by the use of antigens. We have therefore the means of elevating the immunity level of the tissues with which we deal in practice. Inasmuch as it is obviously impossible within the limits of a relatively short paper to deal extensively with the many different types and kinds of infection which the otolaryngologist is called upon to treat, it is considered expedient to discuss but one and to regard it an archetype.

The common acute upper respiratory infection deserves the clinical and investigative attention which it is receiving. It is probable that it is primarily a virus infection. It is a self-limiting disease of brief duration *per se*. Its prolonged course on occasion is due to secondarily invading bacteria, and this secondary invasion should be considered as a complication in the same sense that acute sinusitis or otitis media is considered a complication. There is no known immunity therapy for the primary virus infection. However, it is possible to raise the level of immunity to the secondary complication in an individual subject to these acute upper respiratory infections. The bacteria most commonly found complicating the primary virus infection are the hemolytic staphylococcus, streptococci of various types, pneumococci, and the Pfeiffer bacillus. A choice may be made of one of several antigenic substances in attempting active immuni-

zation: 1) nonspecific proteins, 2) aqueous suspension of killed, whole organisms (vaccines), and 3) filtrates.

Let it be assumed that an effort is made to immunize the individual prophylactically. The choice should be of a vaccine or a filtrate. The filtrates are difficult to prepare, are expensive, and if not properly prepared are valueless. Therefore the vaccine will be more commonly employed. It is necessary to obtain sufficient secretion from all parts of the nose, nasopharynx, and pharynx. This then is cultured on suitable special media. If it is desired to use an autogenous vaccine it is important that the organisms be grown separately after being plated out, and that a relatively accurate estimate of the number of each organism in the vaccine per cc. be determined. For practical purposes a good polyvalent stock vaccine is an adequate and good substitute for the autogenous vaccine. The first consideration in injecting a vaccine is the matter of dosage. A vaccine containing an average of one hundred million bacteria per cc. is too concentrated, and should be diluted from two to five times. The initial dose is a test dose, and should be very small (.05 cc. or less). Upon the character and the extent of the reaction the size of succeeding doses may be estimated. One of several things may occur following the injection of the test dose. There may be: 1) no local reaction, 2) excessive local reaction, 3) general reaction and excessive local reaction, 4) normal reaction.

If there is no local reaction it will be necessary to double or treble the next dose. If there is an excessive local reaction, the next injection will have to be reduced to one-half or one-third of the previous one. An ideal reaction (normal reaction) consists of an erythematous, generally ovoid and slightly raised area at the site of injection, moderately tender to the touch, about 4 cm. in diameter, appearing within 18 hours and generally disappearing within three days. The reaction is devoid of associated general symptoms such as headache, anorexia, malaise, vague muscular and joint pains, rise in temperature, increase in the pulse rate and nasal, nasopharyngeal congestion.

The amount of increase in the size of each succeeding dose should be great enough to insure an adequate normal local reaction. Individuals differ greatly in their sensitivity. The amount of increase is judged on the basis of experience and upon the extent of the reaction to the initial test dose.

*The Selection of the Sites of Injection:* The writer makes a routine practice of making succeeding injections as follows: Right

arm, left arm, right scapular area, left scapular area, right thigh, left thigh, right infracostal area, left infracostal area; then again right arm, left arm, etc. The injections are made intradermally.

*The Interval Between Injections.* The succeeding injections are made when the local signs of the reaction to the previous injection have disappeared, i.e., the redness and the tenderness. In some individuals a slight purplish discoloration may persist for a long time. This is to be disregarded. As one proceeds with the increasing dosage it is preferable to step down from the higher dilutions in order to administer less volume at any one time, thereby diminishing the pain attendant upon the injection.

The question arises, how does one determine when to discontinue the injections? At this point a practical rule of thumb suffices. It is as follows: The injections are discontinued when an injection of 1 cc. of vaccine containing approximately one hundred million of each organism per cc. of vaccine produces a local reaction not much greater than that which was produced by the initial dose of the diluted vaccine. This is an approximation, and there are individuals in whom it is impossible to produce a moderate reaction with the maximum dose. Under these circumstances it is well to discontinue the injections after four or five maximum doses.

Coincidental with the injections of antigen, applications of the antigen are made to the nose and the nasopharyngeal mucosa. An understanding of the implications of the procedure calls for an understanding of the facts of local tissue immunity. Suffice it to say that the same vaccine which has been injected into the patient is applied to the mucosa of the nose and the nasopharynx. The vaccine may be dropped or sprayed into the nose in small amounts (three to four drops daily). However, it has been shown that some irritation of the mucosa enhances the efficacy of this procedure.

It is therefore suggested that the vaccine be applied on a fairly large tampon in the nose, exerting thereby some pressure on the mucosa with a resulting mild irritation. Inasmuch as it is not always practicable to carry out this procedure daily, the writer allows the patient to instill the vaccine daily, and the tampons are applied every three or four days. This is continued for 14 days; then an interval of 14 days is allowed to elapse with no treatment. The treatment is then instituted for another two weeks.

What can be said of the results from such procedures? An opinion based upon sound statistical interpretation is exceedingly difficult to form, as it is in any purely clinical study. These diffi-

culties are too well understood to call for an elaboration here. The writer will merely state his conclusions knowing full well that they will be subject to criticism and realizing that "conclusions" will be regarded as an unwarranted term. The term "clinical impressions," a more cautious phrase, may be more acceptable. The patient with a history of frequent, severe, disabling upper respiratory infection, with or without subclinical low-grade suppurative disease of the sinuses, is benefited by vaccine therapy to the extent that, 1) the infections are less frequent; 2) there is great moderation of the severity of the infections; 3) the period of disability is greatly reduced; and 4) the incidence of complications such as otitis media, and subacute suppurative sinus disease is reduced to a minimum. The writer has never seen an otitis media complicating an upper respiratory infection in a patient who has received adequate prophylactic vaccine therapy within two years. This includes a period of 25 years of experience.

What can be said concerning the active treatment of chronic suppurative sinus disease, chronic suppurative mastoiditis, and chronic suppurative otitis media from the standpoint of immunologic therapy? It is assumed that the clinician sees the matter as a whole and in the light of common sense, with a rational weighing of indications for surgery, or other measures. Under the circumstances it is the conservative judgment of the writer that immunization is an adjunct of signal value and importance. The use, for example, of properly prepared bacterial filtrates as wet dressings is stupidly neglected. Very little clinical study of the applications of the ideas of Besredka in otolaryngologic practice has taken place. The filtrates are not easy to prepare properly. Their clinical possibilities are relatively unexplored, perhaps for that reason.

#### CONCLUSIONS

The writer believes that the otolaryngologist as an immunologist may tend to be replaced by the otolaryngologist as a chemotherapist. This is an unfortunate tendency inasmuch as the study of the phenomena of immunization has never received adequate emphasis in clinical otolaryngology. Clinical immunologic technic has therefore lacked full investigation and subsequent development in this special field. It is the firm conviction of the writer that despite sulfanilamide and similar drugs, it is still true that "the physician of the future will be an immunologist."

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FURTHER MODIFICATIONS OF THE NASAL  
CONTACT TEST FOR ALLERGY\*

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It has long been known that the skin is not completely satisfactory as a diagnostic site in allergic conditions. Reactions to inhalant allergens especially pollens are more reliable than foods; that is, positive reactions are more apt to be true positives, indicative of trouble, and there are fewer false negatives. Even with inhalants the information obtained leaves something to be desired. Various reasons account for this. Dean<sup>1</sup> calls attention to the marked differences in the structure and physiology of the mucous membranes as compared with the skin, which would lead one to expect differences in their reactions to irritants. This is borne out by the observations of Duncan<sup>2</sup> and Cooper,<sup>3</sup> who showed that poison ivy leaf may be chewed with impunity by susceptible persons but contact with the skin about the mouth results in a severe reaction. The same food allergen may cause the most diverse symptoms in different individuals, i.e., may affect only certain cells. Furthermore investigation by Grow and Herman<sup>4</sup> demonstrated that endermal or scratch tests are positive in many perfectly normal individuals, a finding corroborated by Rackemann and Simon.<sup>5</sup>

In addition, in many cases the skin does not lend itself to testing. Among the conditions in which skin tests are difficult or impossible may be mentioned dermographism, ichthyosis, acute or chronic eczema with or without secondary infection, and hyperpigmentation.

In order to obviate these difficulties various methods of applying the antigen directly to the mucosa to be tested have been devised. Kirkman<sup>6</sup> (1835), a sufferer from hay fever, tested himself by

\*Presented before The American Laryngological, Rhinological and Otological Society, New York, N. Y., June 8, 1940.

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sniffing the pollen of sweet vernal grass. He promptly developed hay fever. Blackley<sup>7</sup> tested pollens in the same manner and by introducing small amounts on the conjunctiva, a technique refined by Peshkin.<sup>8</sup> Dunbar,<sup>9</sup> also a hay fever victim, placed the pollens on the mucous membranes by means of little rods or brushes, a method which did not totally exclude the possibility of mechanical irritation. Therefore in order to exclude this objection the hay fever patients sat in a glass cage into which pollen was dusted; with this method also, attacks of hay fever were produced while normal persons who had placed themselves in the experimental cage at the same time showed no evidence of irritation. In addition to using the pure pollen Dunbar also used solutions of "pollen toxin," a protein fraction, with the same results.

In 1923 Duke<sup>10</sup> suggested the use of the nasal contact test as a routine procedure. He did not limit himself to the study of pollens but had the patient inhale from a variety of substances to be tested, noting whether sneezing or other symptoms resembling hay fever or asthma supervened. As an example he described a carpenter troubled with nasal and bronchial symptoms while at work. When he inhaled from a bag of birch wood shavings he had a violent attack of sneezing. The shavings of several other kinds of wood caused no symptoms. Duke<sup>11</sup> observed similar reactions to feathers, furs, perfumes, cedar oil, turpentine and smoke. Efron and Penfound<sup>12</sup> (1930) again proposed the nasal test in the diagnosis of pollinosis. Their work was done entirely with pollens. Using a De Vilbiss powder blower, they blew small amounts of dried pollen into one side of the nose, outside of the pollen season. Suffusion of the eyes, slight burning and tingling in the nose and in more pronounced cases tingling pains at the vertex, slight increase in mucus in the nose and a few sneezes were produced. If the pollen was nonallergenic for the particular patient, symptoms subsided within a few minutes. If it was allergenic, hay fever symptoms of varying severity ensued. As a rule symptoms were of short duration, though one person experienced hay fever for two weeks following the test. This particular test has the objectionable feature of applying too much pollen to the nose.

Rudolph and Cohen<sup>13</sup> (1934) suggested a different method of testing which they had applied to persons with vasomotor rhinitis, whose skin reactions had been negative. The allergen was sprinkled on a pledget of cotton slightly moistened with saline and inserted on a probe held against the mucosa of the middle turbinate and the nasal septum. A control probe with saline was applied to the oppo-

site side. Contact was maintained for 20 minutes, after which the pledgets were removed.

Immediate mechanical reaction which occurs in such cases consists of suffusion of the eyes and irritation of the nose. There may be burning, tingling, and even pain over the bridge of the nose with some mucous secretion and occasionally a sneeze or two. Examination of the nose at this time shows a highly congested mucosa. If the individual is not sensitized symptoms subside in several minutes. In the presence of allergy typical vasomotor rhinitis on the tested side ensues. Reactions are controlled with ephedrine. Occasionally the reaction is prolonged, with nasal obstruction which in one case lasted an entire week.

This technique was also used by Urbach<sup>14</sup> (1935). It is felt that this test, although informative, introduces the element of possible local trauma.

Hansel<sup>15</sup> uses a wisp of cotton twisted loosely on the end of a toothpick, leaving evenly frayed edges, a miniature powder puff. The dry powder puff is dipped into the test substance and the patient takes a short sharp sniff. The powder disappears promptly from the puff, aspirated into the nose, where it is deposited on the nasal mucosa. This test is quite an improvement but uses fairly large amounts of material; hence one may have reactions.

Dean and Linton<sup>16</sup> have employed intramucosal testing. A special 26-gauge gold dental needle with a 30° angle 15 mm. from the end is fitted on a tuberculin syringe. Injections are made under direct vision. Tests are made between episodes of acute rhinitis. The surface of the turbinate is swabbed with 1% cocaine solution; .01 cc. of the test solution is introduced into the inferior turbinate, a pledget of cotton catching the droplet of blood which usually exudes. The patient is observed for 30 minutes to one hour and he reports at the next visit any delayed reactions. Both sides are used simultaneously. The mucosal scratch test is similar to the skin scratch test. One scratch or intramucosal control should be done. A positive reaction is usually indicated by some local edema and swelling of the turbinate in 15 to 30 minutes. At times a perfect wheal is produced. Later symptoms consist of nasal blockage, increased nasal secretion which may simulate nasal hydrorrhea, sneezing, headache, asthma or other symptoms characteristic of the case. Delayed reactions occur. No severe reactions occurred though nasal packs with adrenalin were required in one case. Dean recommends that preliminary skin tests or passive transfer be done. Foods as

well as inhalants are used. They have employed the test in over 1,000 cases with no deleterious results.

#### APPARATUS

The materials required are of the simplest type and are quite inexpensive. We are using a method devised by Dr. David Pipes, formerly of this clinic, to bring the allergen in contact with the nasal mucosa. A benzedrine or similar type inhalator is sectioned transversely. Glass tubes of suitable caliber (those having a diameter of one-half inch are ideal), and about four inches in length are used. The material for testing is placed in the tube, small pledgets of gauze being placed at either end of the test material. This serves as a filter thereby removing the larger particles and reducing the possibility of mechanical irritation. The nosepiece end of the inhalator is fitted loosely over one end of the tube; this permits its removal for sterilization before use. The opposite end of the inhalator is held in place with adhesive plaster. On the adhesive is written the name of the test substance. The tubes containing routine materials are conveniently kept in a wire rack, such as may be obtained in a dime store. Tea-balls and ointment jars half filled with dust or powder may be shaken and inhaled before the particulate matter has settled. A photographer's chromium plated ferrotype squeegee plate is used as the mirror. A stop watch is also required. Glassine paper and china marking pencil are necessary if it is desired to keep permanent records.

#### TECHNIQUE

In 1903 Glatzel<sup>17</sup> described the use of a nickel plated steel mirror to determine the degree of patency of the nasal passages before or after operation. The test was qualitative only at this stage and was of no great practical value. It was rescued from this obscurity by the diligence of Lieb and Mulinos,<sup>18</sup> who saw in it a means of quantitatively determining the degree of dilatation of the nasal passages. They have considerably modified the mirror in ways which we need not go into since the use of a simple plate is entirely feasible from a clinical point of view. After allowing the individual to breathe on the plate Lieb and Mulinos then quantitatively determined the areas of moisture deposited with a planimeter. By measuring the time of evaporation with a stop watch they obtained an accurate measure of the quantity of air passing through each nostril. These authors photographed the areas of moisture, a refinement not necessary clinically.

In previous methods of nasal contact testing it was not possible to test in the presence of active nasal allergy since a positive reaction would not necessarily increase symptoms already present, and in the presence of objective signs there was no way by which one could distinguish between a positive and a negative response. With the mirror however the test may be employed in acute rhinitis provided both nostrils are sufficiently patent to allow air to flow through them. With a nasal speculum the mucosa is examined. A reacting mucosa is pale, sometimes almost pearly, more or less edematous, often with increased mucus.

The mirror, which has been kept in the icebox, is allowed to warm to an extent sufficient to permit evaporation of the moisture which invariably condenses. The evaporation time varies but averages from 100 to 200 seconds. The plate is then held horizontally under the subject's nostrils, the mouth being shut, and he is allowed to exhale on the mirror five times. The plate is then withdrawn and the stop watch started. It is our practice to outline the areas of moisture, which somewhat resemble a butterfly's wings, with a china marking pencil. At a later time one may then trace over these with glassine paper, thus obtaining a permanent record. By means of the stop watch the time required for each side to evaporate is determined. The plate is then returned to the icebox. The more patent nostril is chosen for the test site. With the finger apposed to the opposite nostril, the nosepiece end of the inhalator is inserted and the patient then inhales three or four times. As a rule there is no ensuing mechanical or immediate reaction, though occasionally in strongly allergic individuals there may be sneezing and rarely a sense of stuffiness or pain. If there is any sneezing there may be slight temporary conjunctival congestion. At the end of fifteen minutes the nasal mucosa is again examined with the aid of the speculum. In a positive reaction there may be beginning edema with pallor and increased secretion. There may be sneezing, rhinorrhea or even lachrimation. The same mirror, or another, having been removed from the icebox, is used as before. The areas of moisture are again outlined and the evaporation time for each nostril determined.

#### DISCUSSION

The interpretation of the test is based on a simple computation. The evaporation time in seconds of the more patent side (numerator) is divided by the evaporation time of the other side (denominator). After the test, the same sides are used as numerator and denominator but the new values are substituted.

We feel that a minimal change of 25% in the time consumed by the evaporation of the areas of moisture is a requisite for a positive diagnosis, but here as in other allergic tests, all degrees of positivity are encountered. At times there is a complete obstruction and no air passes through the tested side. This may be referred to as a four-plus reaction. Again, the reduction may be half this extent, a two-plus, and so forth. As is true of all allergic tests delayed reactions sometimes occur.

The record of each test should include description of the nasal mucosa before the inhalation and again after fifteen minutes; the occurrence of sneezing, itching, stuffiness, rhinorrhea or lacrimation, especially after five minutes; the time required for evaporation of each area of moisture before inhalation of the test substance; tracings of each area with glassine paper; and when possible, in positive cases, record of smear eosinophil count at the height of the reaction.

The test as described is relatively quantitative in contrast to the relatively qualitative test by inspection only. Greater accuracy is obtained, positive reactions often being determined by the mirror where negative responses would have been diagnosed by direct inspection. Slight changes will sometimes involve the entire nose to a grossly imperceptible amount, yet there will be a degree of obstruction detectable by the mirror. Again, the obstruction may be invisible through involvement of the posterosuperior portion of the nose. In addition, when the test is only moderately positive the patient is unaware of any change.

At times one nostril is completely obstructed and in these instances the test may not be used, although direct observation of the mucosa is not precluded. Obstruction may be due to hypertrophic turbinates, multiple polyps and in one of our cases to a repaired cleft palate. Very hot weather impedes the use of the test because of the rapid evaporation of the areas of condensation. Only a few tests can be done at any given time, hence they are time-consuming. The patient may be inconvenienced by the production of the actual disease. In one case an attack of asthma of short duration was produced by the inhalation of dust, although the nasal contact test was negative. It may be stated that we do not use pollens because of the severe reactions encountered and because accurate information as to mucosal sensitization may be readily obtained by means of the conjunctival test. We employ the pure substances in their natural state and not highly concentrated; in this way prolonged reactions are avoided.

In spite of the disadvantages listed above the nasal contact test is a useful adjunct in the diagnosis of respiratory allergy. It is physiologic in its approach and tends to reproduce the natural conditions productive of symptoms. It detects false positive and false negative skin reactions. The fact that skin tests, either scratch or endermal, have been positive does not control the selection of nasal contact tests. We have seen three- or four-plus endermal or even scratch reactions to allergens such as house dust, feathers, orris root, and tobacco entirely negative by nasal contact, and vice versa. This is important since if direct application of orris root to the nasal mucosa does not cause symptoms in a case of nasal allergy one need not put the patient to the bother of being desensitized to orris root or avoiding it. As a consequence our routine is to test by the nasal contact method to the more common allergens such as dust, feathers, orris root, tobacco, silk, and pyrethrum. Occasionally others such as horse dander, rabbit hair and cat hair may be used. The test may be used where the substance to be tested can be extracted only with difficulty, such as odors, or when the patient does not wish to destroy some article for the purpose of extraction. This was true in one instance in which a strongly positive nasal contact was obtained to a beautiful angora sweater, the disposal of which was accompanied by the disappearance of the lady's symptoms.

In a criticism of nasal contact tests in general Walzer and Thommen<sup>10</sup> stated that the main symptoms of the test, sneezing and nasal congestion, may be more subjective than objective, a fact which considerably detracts from the value of the test. A further disadvantage according to these authors, is the difficulty of inspecting the reaction inside the nose. We feel that these objections at least have been obviated by the use of the mirror.

Finally the inexpensiveness and availability of the materials required, and the information so readily obtained strongly recommend the test as a routine adjunct in cases of respiratory allergy. The test is not offered to supersede other diagnostic procedures, but it is felt that it is a worthwhile addition.

#### SUMMARY

A modification of the nasal contact test is proposed. This entails the use of a mirror, originally devised by Glatzel, and a quantitative test by Lieb and Mulinos. A new method of applying the allergens to the nasal mucosa is described.

## CASE 1

BEFORE



AFTER



## CASE 3

BEFORE



AFTER



## CASE 5

BEFORE



AFTER



## CASE 2

BEFORE



AFTER



## CASE 4

BEFORE



AFTER



## CASE 6

BEFORE



AFTER



Outlines of areas of condensation before and after inhalation of test material.



## ILLUSTRATIVE EXAMPLES

## Case 1

Pt.: Master D. R.

Substance: House dust

Side tested: Left

Evaporation time (in seconds) before: R:70" L:105". After R:150"  
L:105"

Factor (determined by dividing numerator, i.e., more patent side,  
by denominator, i.e., less patent side, and multiplying the divi-  
dend by 100. In the case above  $105 \times 100 = 150$ ) before: 150  
after: 70 70

Interpretation: Two plus.

## Case 2

Pt.: Mrs. N. R. H.

Substance: Orris root

Side tested: Left

Evaporation time (in seconds) before: R:130" L:135". After R:140"  
L:25"

Factor before: 103, after 18

Interpretation: Three plus.

## Case 3

Pt.: Mrs. R. D.

Substance: Feathers

Side tested: Right

Evaporation time (in seconds) before: R:55" L:55". After R:120"  
L:125"

Factor before: 100, after 96

Interpretation: Negative.

## Case 4

Pt.: Mr. J. R. H.

Substance: Dog hair

Side tested: Right

Evaporation time (in seconds) before: R:80" L:80". After R:45"  
L:75"

Factor before: 100, after 60

Interpretation: One plus.

## Case 5

Pt.: Miss E. G.

Substance: Wool

Side tested: Right

Evaporation time (in seconds) before: R:145" L:105". After R:40"  
L:170"

Factor before: 138, after 23

Interpretation: Three plus.

## Case 6

Pt.: Miss A. O'N.

Substance: Orris root

Side tested: Right

Evaporation time (in seconds) before: R:135" L:115". After R:0"  
L:150"

Factor before: 117, after: Infinity

Interpretation: Four plus

## SAMPLE RECORD FORM

Name \_\_\_\_\_ Record No. \_\_\_\_\_ Date \_\_\_\_\_

*Nasal Contact Tests*

Substance: \_\_\_\_\_ History: \_\_\_\_\_

Side Tested: \_\_\_\_\_ Scratch: \_\_\_\_\_

Endermal: \_\_\_\_\_

Evaporation Time R L

Factor Before

Evaporation Time

Factor After

Interpretation

Eosinophil Smear Count

Appearance Before Appearance After

Time: Time:

Subjective: Sneezing, swelling, itching, nose running \_\_\_\_\_

Objective: \_\_\_\_\_

Delayed Reaction: \_\_\_\_\_

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## LXXXIX

### POSTTRAUMATIC SYNDROME OF HEAD INJURY\*

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Before discussing the more specific symptoms which may follow blows to the head, I should like to review briefly the physiopathologic changes associated with head injury. We may classify injuries to the brain, according to their severity, under the headings concussion, contusion, and laceration.

Concussion can be defined as an unconscious state caused by a temporary physiological disturbance of cortical function, without the production of a pathological lesion. Contusion may be identified with a more protracted period of unconsciousness, with a tendency toward the development of focal signs resulting from pathological changes in the brain. Laceration needs no further definition; it implies extensive damage to the brain.

Much speculation has been aroused and many theories have been advanced as to the physiology of unconsciousness resulting from head injury. One accepted by many is based upon the production of an acute cerebral anemia. At the moment of impact, the skull, because of a slight elasticity, is flattened at the point of impact and the intracranial volume is momentarily increased. It is contended that this sudden alteration produces an acute cerebral anemia with immediate unconsciousness. Duret, years ago, offered the hypothesis that this rapid compression of the cranial content forced the cerebrospinal fluid from the ventricles through the narrow aqueduct of Sylvius, damaging the structures in this area and causing a reflex cerebral anemia. This has been disproved by subsequent experiments. The cerebrospinal fluid was aspirated from the ventricles, and it was found that unconsciousness could be produced by the application of the same force to the head that had been required before withdrawal of the ventricular fluid. Koch and Filehne showed that repeated light blows to the head, not sufficient to alter the shape of the skull, would produce unconsciousness which they

\*From the Department of Surgery, University of California Medical School. Read before the Western Section Meeting of the American Laryngological, Rhinological and Otolological Society, San Francisco, Calif., February 2, 1941.

believed to be the result of a molecular disturbance in the brain cells, through the application of mechanical forces. Miller's work seemed to support this belief. In his opinion, anemia could not produce the immediate loss of consciousness present in concussion. He was able to demonstrate in the frog that, after removal of the heart, consciousness was still present and that unconsciousness could then be produced by a blow to the head, followed by a subsequent return of the conscious state. His further experimental work in which, under local anesthesia, the aorta of the rabbit was clamped off for five seconds without loss of consciousness, is additional evidence against the theory of cerebral anemia. It is his belief that the unconscious state is the result of an actual disturbance of the equilibrium and function of the brain cells, resulting from the widespread effect of the force of the blow. It would appear that there is considerable evidence to support this theory regarding the physiology of concussion.

Many observers consider concussion and contusion of the brain as synonymous terms. In their opinion any blow sufficient to cause unconsciousness is sufficient to produce some pathological changes in the brain, even though they are of microscopic size and perhaps insufficient to produce subsequent neurological findings. Miller was able to show, in rabbits, that concussion is possible without demonstrable pathological changes in the brain. It is obvious that clinically we are not always able to draw a fine line of distinction between concussion and contusion. It has often been said that unconsciousness must be present to justify a diagnosis of concussion or contusion of the brain. I believe that such a statement is inaccurate and often leads to errors in diagnosis with gross injustice to patients. A careful evaluation of the conscious state following head injury can be had only by questioning the patient as to the events immediately preceding the injury and subsequent to it. It is not uncommon to have a patient say that he was not unconscious, but further inquiry may bring out the fact that he has a short retrograde amnesia for events preceding the blow, nor can he recall with clarity the details for a short time thereafter. Such information indicates a disturbance in the conscious state without a complete loss of consciousness. A classical example is that of the football player who receives a blow to the head but continues to play until his teammates note that he is behaving in an abnormal manner. He is taken out of the game and later will have no recollection of playing at all despite the fact that he was on his feet and going through maneuvers in a more or less reflex manner. Such patients may suffer serious injuries with actual contusion of the brain and pathological changes demonstrable

on neurological examination. Prolonged symptoms which are out of proportion to the apparent severity of the original injury may result in such cases.

The actual presence or absence of a fracture of the skull is of secondary importance, with certain special exceptions. Depressed fractures require early diagnosis and treatment as do those involving the frontal sinus. Basal fractures with escape of cerebrospinal fluid from the ear also require special attention. It is not within the scope of this paper to discuss the phase of early treatment, but I should like to comment on the role of chemotherapy in these cases. The likelihood of meningitis is considerable in cases of cerebrospinal rhinorrhea or otorrhea, or in those in which there has been free bleeding from the ear. Since the advent of sulfanilamide and sulfapyridine as prophylactic drugs, I have not encountered complicating meningitis if adequate treatment was instituted promptly.

Before proceeding to the more specific symptoms following head injury, I should like to discuss briefly the general care of such patients. It is highly important to keep them at rest for rather long periods of time depending upon the severity of the injury. This should include the removal of outside worries and anxiety as nearly as possible, and the avoidance of frequent visiting with relatives. The attending physician should build up an optimistic outlook for the future, minimize the importance of symptoms as much as possible, and avoid a discussion of the case in front of the patient, particularly with reference to any mention of a fractured skull or an injury to the brain. A proper mental attitude is essential for recovery in any patient with a head injury and may be an important factor in avoiding some of the symptoms so frequently seen after these injuries.

An early complete neurological examination of all patients with head injury is essential in the evaluation of late symptoms that may either persist or appear at a later time. The presence of obvious disturbances in the cranial nerves or alterations in motor or sensory function or reflexes probably indicate that organic changes have occurred, though many of these patients make an apparently complete recovery. An otological examination should be conducted as soon as possible if there is evidence of injury either to the vestibular or auditory portions of the eighth nerve. Unfortunately certain factors may delay such studies. The patient's mental state, the inability to move him about or the danger in any manipulation of the ear if there has been frank bleeding or escape of spinal fluid may necessi-

tate considerable delay in the evaluation of the otological status of the patient.

Thus far we have considered some phases of the problem that precede the so-called posttraumatic syndrome. Many names have been applied to this group of symptoms which are all too frequently encountered following trauma to the head. Personally, I do not believe that the nomenclature employed is of great importance. What we are interested in is whether the complaints arise from organic changes in the central nervous system, or are functional or hysterical in nature, or whether we are dealing with gross exaggeration or malingering, arising from a desire to gain something. In some instances the history of severe injury and the presence of objective neurological findings indicate at once an organic basis to substantiate the subjective symptoms. Unfortunately, however, the majority of these patients have no positive findings and their classification becomes extremely difficult.

The subjective complaints are numerous. The commoner ones are headache, dizziness, nervousness, tinnitus, impaired hearing, impaired memory, irritability, emotional instability, fatigability, and faulty concentration. What means have we at our disposal to reach a final conclusion? Patients in whom the diagnosis is questionable should be hospitalized for complete study. This consists of a complete general physical examination to rule out any coincidental disease, a complete neurological examination with subsequent re-examination to determine the presence of objective neurological findings, spinal puncture with pressure readings to determine the presence or absence of increased intracranial pressure, and encephalograms to determine the presence or absence of any gross lesion such as subdural hematoma, arachnoidal adhesions, cortical atrophy or scars of the brain with resulting deformity of the ventricular system. Pathological changes may be found in the encephalographic studies despite a completely negative neurological examination, and their presence will supply a definite basis for the subjective complaints. In some instances the pathological changes demonstrated by encephalography allow the institution of further treatment on a more rational basis. A subdural hematoma can be evacuated surgically, excessive sub-arachnoidal or subdural accumulations of fluid may be treated by dehydration or, occasionally, drained externally as the situation demands. Cortical scars with traction on the ventricular system may be excised with improvement in or relief of symptoms. Unfortunately, the structure of the central nervous system is so constituted that it has no ability to regenerate. If the neurological examination

or the encephalograms indicate actual damage to or destruction of certain areas of the brain, we are dealing with an irreversible process that forecasts some degree of permanent loss of function.

Careful otologic studies may reveal pathological changes after all other methods have failed. Linthicum and Rand reported studies on 36 patients with cerebral concussion who complained of dizziness. These were divided into (1) those having a true vertigo, with which the patient actually complains of rotation of objects about him, associated with nystagmus at the time, and which probably originates in the end-organ; and (2) those having false vertigo described by the patient as a sense of uncertainty, confusion, or light-headedness, which Linthicum and Rand indicated might be ocular or intracranial, involving the vestibular tracts. The majority of the patients complained of false vertigo and in each these authors found some evidence of labyrinthine abnormality, the commonest finding being that of altered pastpointing, which was present in every case.

Brunner called attention to a decrease in or an absence of caloric response on one side which, he said, might be the only finding to indicate the presence of an organic basis for the symptoms.

Grove reported extensively on the otological aspects of head injury. In 150 cases he reviewed, 32% of the patients showed some otological signs or symptoms. His studies of the labyrinth showed, as also reported by others, that either hypo-irritability or hyper-irritability may be present. In his opinion the lack of balance between the two labyrinths is responsible for the subjective complaints of the patient.

If, after such exhaustive studies, no positive findings are forthcoming we must conclude that there is no organic basis for the complaint. The condition then is either functional or to be attributed to malingering. Differentiation between these two conditions requires careful thought and study. The patient's background and previous nervous make-up, family, outside influences, litigation, compensation, mental attitude and desire to get well, all must be taken into account in so far as possible before a final opinion is given. Fortunately frank malingering is not common and the symptoms of functional nature tend to subside rapidly with the removal of anxiety, settlement of litigation or compensation aspects, and return to regular employment.

I should like to consider a few of the more specific symptoms that may be encountered in the field of otology and rhinology. Dis-



turbances of the sense of taste and smell have not received a great deal of attention in the literature, although they are often very distressing to the patient. Alterations in the sense of smell are much more frequent than those of taste, and are often seen in connection with fractures through the cribriform plate and the floor of the anterior fossa. Not infrequently they follow injury without any demonstrable fracture, apparently resulting from local damage to the olfactory bulbs and their connections. The loss may be partial or complete, unilateral or bilateral, and if complete, produces an apparent disturbance in the sense of taste as well. A good deal of our appreciation of taste results from the impression made on the olfactory sense, particularly with reference to aromatics and highly seasoned foods. Consequently, with the loss of smell, many foods lose the attractiveness which we ordinarily think of as resulting purely from taste. A partial loss of the sense of smell may show improvement or recovery but if a complete anosmia exists little promise can be given for restoration of function.

The disturbance of taste may result from damage to the seventh nerve or chorda tympani; this is usually unilateral, is seldom sufficiently complete to produce many subjective complaints and frequently spontaneous recovery follows. In a few instances, I have encountered a complete loss of gustatory sense. It has been suggested that this may result from rather severe damage to the anterior portion of the temporal lobes, although it is by no means certain. In any event, these patients are greatly distressed by this loss and complain that they have no appetite for or enjoyment of food and are guided to meals merely by the clock and the gastric pangs indicative of an empty stomach. The condition is permanent in most instances.

Fractures through the petrous bone may produce severe and disabling symptoms. Such fractures have been divided into (1) longitudinal fractures, the more common type, which are frequently associated with bleeding from the external ear and which may produce a subtotal loss of hearing but do not damage the labyrinthine capsule, and (2) transverse fractures, which are much easier to visualize by X-ray, result in a higher percentage and more severe loss of hearing and may involve the labyrinth.

Damage to the labyrinth occurs more frequently as a result of concomitant concussion rather than of direct damage by the fracture line, and it may occur without fracture. Brunner stressed the point that concussion of the inner ear results in acutely increased pressure with damage to the *sacculus endolymphaticus* and lymph channels.

Accumulations of lymphocytes and transudates may occur in the inner ear producing further symptoms. The eighth nerve may also be damaged within the brain stem itself or along the intracranial course of the nerve as well as in its more peripheral distribution in the petrous bone. Its short course and fixed position as it passes into the internal auditory canal make it susceptible to stretching injury when the brain is subjected to sudden movement during a head injury. Damage to the vestibular or the auditory portions of the eighth nerve, the cochlea or the labyrinth often produces distressing and disabling symptoms which can be demonstrated by a careful otological study and leave no doubt as to the authenticity of subjective complaints. Fletcher stressed the value of these studies in appraising symptoms in cases of industrial injury and, contrary to some observers, found that losses of hearing may be more difficult to evaluate than vestibular disturbances.

Persistent vertigo may completely disable a patient for all activity, and treatment is often inadequate. The restriction of sodium in the diet and the use of ammonium chloride by mouth have been suggested by Furstenberg in the treatment of Ménière's syndrome. I have had no real success with this method in treating the vertigo which may follow injury. Section of the eighth nerve intracranially has been employed a few times but not with any uniformly satisfactory results. In this connection, we must bear in mind that the damage to the eighth nerve may have occurred in the brain stem or associated pathways and, in such cases, a section of the nerve would be peripheral to the pathological process and therefore valueless. Surgical destruction of the labyrinth itself also appears to have little to recommend it in the treatment of posttraumatic vertigo. In my experience, this symptom has shown a gradual tendency to decrease over a period of months or years, with complete recovery in many; a few, however, have still had a disabling degree of vertigo after several years.

Fracture through the petrous bone may also result in damage to the seventh nerve with facial palsy. The palsies which appear immediately may be caused by a severance of the nerve and the prognosis in these cases should be guarded. More frequently the palsy does not appear until from one to four days after injury, in which case it has resulted from hemorrhage around the sheath of the nerve. The majority of these patients recover spontaneously over a period of several weeks, requiring only support of the muscles and perhaps gentle massage.

I have had the good fortune to observe the majority of repairs of the facial nerve done by Martin in cases in which facial palsy appeared after mastoidectomy. Such surgical exposure of the facial nerve may be indicated for patients in whom spontaneous recovery of facial palsy resulting from petrous fracture fails to occur. If damage has been done to an accessible portion of the nerve, suture or neurolysis may result in a return of function.

In conclusion, I should like to stress the following points: The evaluation of head injuries and the posttraumatic symptoms which follow them require a careful analysis of the patient's injury, early course, subsequent neurological findings and, in some instances, spinal puncture and encephalographic studies. Otolological examination is essential if there is any suggestion of auditory or vestibular disturbance. In addition to this information, we must take into account the patient's age, general physical condition, previous nervous make-up and outside influences such as compensation and litigation. It is only by a complete survey of all of these factors that we can hope to reach a conclusion as to whether we are dealing with an organic condition, a functional state, or malingering, and be able to give a reasonable prognosis as well as advice with regard to the patient's future.

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COCAINE ADDICTION: DOES IT CONCERN  
THE OTOLARYNGOLOGIST?\*

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It is a common belief among the laity, and to some extent among the medical profession, that a large number of people in the United States are addicted to the use of cocaine, either for its supposed pleasurable effects or for the relief of pain and discomfort in the nose and paranasal sinuses. Nose and throat specialists at times have been accused<sup>1</sup> of producing the cocaine habit by the frequent use of cocaine sprays or packs in the noses of patients suffering pain from nasal sinus infection or from some form of nasal neurosis. Most otolaryngologists use cocaine daily in their practice for its rapid anesthetic and ischemic effects. While no entirely satisfactory substitute for cocaine has been discovered, some physicians are using other preparations almost entirely. But the majority of otolaryngologists and ophthalmologists employ cocaine in some manner in their practice. Indeed one of the largest clinics in the country still uses cocaine solution for injection for tonsillectomy under local anesthesia.

From his close association with cocaine, from his observation of patients upon whom cocaine is used, and from the fact that drug addicts the country over know that the ear, nose and throat doctor usually has cocaine in his office—from these facts it is reasonable to assume that the otolaryngologist is in a position to judge whether addiction to the use of cocaine is widespread or whether it is relatively rare, and whether the use of cocaine in our practice is playing any part in addiction to the drug.

In gathering information on this subject a number of physicians and druggists were consulted. General practitioners, internists, and psychiatrists were consulted locally. Correspondence was entered into with otolaryngologists and superintendents of hospitals for nervous and mental diseases in different parts of the country. Many of the doctors interviewed believed that the incidence of cocaine addic-

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\*Presented before the Southern Section of the American Laryngological, Rhinological and Otological Society, Nashville, Tenn., January 8, 1941.

tion is high; others had no definite opinion as to incidence. Almost without exception they all stated at first that cocaine addiction was prevalent in the United States. After explaining that I was attempting to find out about the misuse of cocaine only, and that I was not interested in other forms of drug addiction such as alcoholism and morphinism, none of the doctors or druggists had personal knowledge of a single case of pure cocaine addiction. There were some cases of alcoholism and morphinism, particularly the former, when the patient would take any drug he could obtain, such as veronal, trional, luminal, cocaine, and bromides, while on a debauch. Many of the older doctors and the older pharmacists could recall specific instances of cocaine sniffing, particularly among negroes, before the passage of the Harrison Narcotic Act in 1914. The records of nearly 5,000 patients in the South Carolina State Hospital show many drug addicts among the inmates. However, there is no record of any patient using cocaine by itself, although there are some patients who used "all drugs" according to the information as recorded.

An interesting point brought out in this investigation was the fact that several of the younger practitioners interviewed had not considered cocaine as a drug with habit-forming properties. These physicians were very keenly alive to the problem of drug addiction as it relates to alcohol and the opium derivatives. They had all had considerable experience with alcoholics and "dope fiends." But the likelihood of cocaine being used by any of these addicts had not been given a second thought.

As far back as 1925 the use of cocaine for other than medicinal purposes was not considered to be a problem in the United States. In his report on "The Legal Use of Narcotics in Detroit, Michigan and Environs for 1925-26," Dr. C. E. Terry<sup>2</sup> in summarizing the conclusion of the investigating committee states: "The misuse of cocaine does not constitute a medical problem in the localities studied." The United States Treasury Department, Bureau of Narcotics in its report on "Traffic in Opium and Other Dangerous Drugs"<sup>3</sup> for 1933 shows that the amount of cocaine being smuggled into this country is negligible as compared to morphine and heroin.

Dr. W. E. Dixon<sup>1</sup> of Cambridge University says: "Cocaine as a drug of addiction came into notice in the early nineties, but the habit of sniffing became in no sense a menace till about 1910. In the early days of the war cocaine users became plentiful in Paris; the alkaloid could be purchased from the habitués of the cafés and music-halls, and the cult of sniffing came into existence, and quickly spread to London. The cocaine was used in these instances, at all

events at first, as a ripid and exhilarating intoxicant, a substance to produce complete abandon and an utter disregard for consequences and the future; more occasionally it was taken in some form of alcoholic beverage. In pre-war days a good deal of addiction has been traced to prescriptions given for the relief of pain or the treatment of disease, such as the use of a cocaine spray for hay fever or asthma. Since the war it is safe to say that addiction to cocaine never follows the physician's prescription."

The New York City Narcotic Clinic, S. Dana Hubbard, M.D., Director, reports:<sup>1</sup> "Some have expressed the thought that cocaine caused a condition in the system requiring its continuance. It has been learned that such is not a fact. On the contrary cocaine is used for a stimulant or antidote to certain undesired after-effects for other drugs—to overcome the drowsy effects of morphia or heroin. \* \* \* Cocaine does not produce in the system a need similar to that from the continued use of morphia. The cocaine habit is like the alcohol habit—the man may want the drug, but if he cannot get it he will, and can easily do without it, and will not have any actual physical misery or distress. \* \* \* Cocaine was distributed on the first day the clinic was operated, but on ascertaining the fact regarding its effect on the individual, it was immediately discontinued and not again prescribed or dispensed."

The usual method of taking cocaine has been by sniffing or snuffing the cocaine crystals or powder into the nostrils where it comes in contact with the nasal mucosa, from which it is very quickly absorbed. This is similar to the old habit of taking snuff. An attempt was made to determine whether there might be any other methods employed in cocaine addiction other than the sniffing of the drug into the nostrils. The South American Indians in Peru are said to chew the coca leaves and also to drink tea made from the coca leaves.<sup>5</sup> Lesions of the oral mucous membrane<sup>6</sup> have been reported among these Indians just as ulcers of the nasal septum were at one time commonly reported among cocaine addicts in America and Europe.<sup>7</sup>

It has been said that some cocaine addicts have taken the drug by drinking it in alcoholic beverages,<sup>1</sup> but I have not been able to find in the literature a specific instance reported in which cocaine was taken in this manner.

Nearly all morphine addicts take their "dope" hypodermically, but this method is apparently never used by the cocaine habitués. Sir Arthur Conan Doyle in one of his early Sherlock Holmes stories,

has his famous detective taking a 6% solution of cocaine by hypodermic injection for its exhilarating effects.<sup>8</sup> Soon after cocaine was discovered in 1884, Professor William S. Halsted of Johns Hopkins Medical School, who was then practicing in New York City, became interested in the anesthetic effects of cocaine. He and his associates, using themselves as subjects for experiments, mapped out the areas of distribution of the cutaneous nerves by injecting the nerve trunks with a solution of cocaine. Dr. Harvey Cushing<sup>9</sup> states that in this way Professor Halsted became addicted to the use of cocaine. Dr. J. M. T. Finney,<sup>10</sup> in writing of this episode in Dr. Halsted's career, says that Dr. Halsted and his associates got the habit by sniffing the drug during the course of their experiments. At this early date little was known of the effects or habit-forming properties of cocaine, and it is only fair to state that in this case the habit was innocently acquired, and that Professor Halsted was later completely cured.

Dr. Lawrence Kolb,<sup>11, 12</sup> Assistant Surgeon General of the U. S. Public Health Service, who is well known for his classification of drug addicts, has written: "You are advised that in my experience pure cocaine addiction is now very rare, if not actually non-existent, in this country. There are, of course, some persons who take cocaine now and then when they can secure it, but cocaine is mostly indulged in by these persons in much the same way as some people get drunk on Saturday or on week-ends. According to studies I made some years ago most persons who start to use cocaine eventually become addicted to morphine or heroin through taking these drugs to relieve themselves from the distressing effects (anxiety and restlessness) caused by cocaine, but even this type of temporary cocaine addiction is now quite rare. I had charge of the Lexington narcotic hospital for three years and during that time there were no cases of pure cocaine addiction admitted and I am not aware of any that have been admitted since then. There were, however, some patients who had indulged in cocaine off and on at some time during their addiction career. It is well known that cocaine does not cause addiction in the sense that it creates a necessity for the continued use of the drug such as is created by opium and its preparations. However, there was a time when many people, thrilled by the stimulating effect of the drug, indulged in its use for other than medical purposes."

My own personal experience with cocaine addiction has been meager. In going over my case records of the past 20 years I was struck with the scarcity of cases which were even questionably diagnosed as drug addicts. There were a few alcoholics both male and female who would come in after a debauch and say that they had a



pain in the head due to "sinus trouble." They would want something put into their nose to relieve the pain, and usually they would suggest that they be given morphine or codeine to take. Then there were a few cases of frank morphine addicts who claimed sinus trouble or trifacial neuralgia. They usually volunteered the information that relief was obtained only by a cocaine pack together with a hypodermic injection of morphine.

There was one patient, a young lady, referred to me as a questionable cocaine addict. She suffered periodic attacks of pain in the left side of her head. She had been told that she had a left-sided pansinusitis. She voluntarily stated that a cocaine spray or pack in her left nostril gave her temporary relief from the pain. Examination revealed no clinical or X-ray evidence of nasal sinus infection. She has since been completely relieved by ergotamine tartrate when her migraine attacks occur.

In the routine daily use of cocaine in the office and hospital I have very rarely observed the stimulating and exhilarating effects of the drug. Nor have I had many patients describe a sense of well-being or euphoria. On the contrary, when sufficient cocaine is used to obtain systemic effects, most patients appear somewhat anxious and restless rather than exhilarated. Many of them feel as if they were going to faint or collapse. This has been the experience of my professional colleagues who have had cocaine used on them for local anesthesia.

The conclusions to be drawn from a review of the literature, from interviews with doctors, druggists, and hospital superintendents, and from personal experience in using cocaine in the practice of otolaryngology, are that:

1. Cocaine addiction is excessively rare in the United States.
2. Otolaryngologists as a group should not be taxed with being instrumental in producing the cocaine habit among certain patients.
3. It is high time for some physicians to revise their ideas as to the habit-forming or addiction properties of cocaine.

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## XCI

### PROPHYLAXIS AND TREATMENT OF THE COMMON COLD WITH SPECIAL REFERENCE TO RESPIRATORY VACCINE

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SPOKANE

There is no uniform conception of the common cold among either members of the profession or laymen, and in taking histories it is necessary to interrogate the patient in detail to ascertain if he is actually subject to head colds. Almost continuous or frequently recurring sniffing due to a persistently thin, serous nasal discharge does not constitute a cold. Acute pharyngitis and tracheitis do not constitute a cold although they may precede or follow acute rhinitis. To my mind a common cold is characterized by a hot, dry feeling in the nose for a few hours, usually overlooked by the patient, followed by sneezing, nasal obstruction and thin, watery nasal discharge for 48 hours, after which the discharge becomes thick and yellowish or greenish, gradually diminishing in the third week of the disease. Sometimes the initial symptom is a hot, caustic post-nasal discharge with marked soreness of the superior surface of the soft palate. Kerr<sup>1</sup> states that a common cold runs its course in three to five days and that longer duration indicates complications. If this be true the uncomplicated cold is of little physical or economic significance, and such colds are probably abortive or due to allergy. The stage of thick discharge is usually accompanied by ethmoid infection, or, much more rarely, involvement of the other sinuses. When the first two stages are absent and symptoms are initiated by a viscid, colored discharge it is indicative of activation of quiescent chronic sinusitis.

In 1932 Thomson and Thomson<sup>2</sup> reviewed 40 reports of vaccine prophylaxis and therapy of respiratory infection. Three-quarters of these authors considered vaccines of definite value. Herewith are reviewed ten reports<sup>3-12</sup> (11 series) of attempted immunization against the common cold showing results as widely divergent as were

the methods of treatment. Four authors conclude that vaccine prophylaxis is ineffectual, while the enthusiasm of the others is graduated from the faint praise of "favorable" to reports showing three times as many colds in the controls as in the vaccinated. It is impossible to draw any conclusion concerning the best type of vaccine or the amount, frequency and method of administration most likely to produce favorable results. Five authors used heat-killed bacteria, three did not state the type of vaccine, while Kreuger type, Rosenow vaccine and dissolved bacterial protein were each used once. In four instances the strength of vaccine was not reported; the strength of two was estimated by nitrogen content, and six had a bacterial count ranging from 800 million per cc. to ten times that strength. In three of these reports the method of administration was subcutaneous; in six it was not stated but was presumably subcutaneous, while one investigator used intradermal injections. Initial dosage varied from 1.0 cc. containing 2020 million bacteria to 0.1 cc. containing 200 million. Two authors did not report the dosage or duration of treatment. In three instances the injections were given throughout the season; one author used six to ten graduated doses; another four injections in autumn and two in mid-winter; while the remaining series employed one to three injections. In only two instances was the relative sensitivity of the individual considered, once, in a seasonal course, where the maximum dose was regulated by the reaction obtained, and once in a two-injection course, when the interval was lengthened if a reaction occurred. Neither report reveals whether greater or less benefit was obtained in the most sensitive subject. There is no factor of type of vaccine, method of administration, dosage or duration of treatment common to the favorable reports to which success may be attributed. Four additional reports are of interest: Stafford<sup>13</sup> and Rockwell<sup>14</sup> concluded that oral vaccine had a marked protective value. I have no experience with this method of prophylaxis, but several patients have told me of considerable benefit obtained from self-administered oral vaccine. This is not, however, council accepted.<sup>16</sup> That it might be efficacious is suggested by the fact that I have known nasal symptoms to be produced by its ingestion. Walsh<sup>15</sup> stated that vaccine sprayed intranasally was effective in 78% of a small series from which persons with chronic nasal defects were excluded. Thomson and Thomson<sup>2</sup> comment favorably on this method.

For seven years I have been using a stock mixed respiratory vaccine of the following content of chemically killed bacteria:

Staph. aureus	600 million
Staph. albus	600 million
Strep. hemolyticus and viridans	200 million
Pneumococci I, II, III, IV	150 million
M. catarrhalis	150 million
Friedlander's b.	150 million
B. influenzae	150 million
<hr/>	
2000 million per cc.	

This vaccine is made locally and is kept potent by the frequent addition of virulent organisms obtained from actively ill individuals. If a new lot of vaccine is employed during a course of treatment it is usually necessary to decrease the dose to avoid reactions. In the prevention of acute rhinitis I believe that the vaccine should be given intradermally, that the initial dose should be small, that treatment should be carried on throughout the winter season, that only sensitive individuals are benefited, that the dosage must be individualized and that, although freedom from acute rhinitis may frequently be achieved, there is no immunity against pharyngitis, laryngitis and the descending type of chest cold.

The results obtained from a short series of subcutaneous injections (0.1 to 1.0 cc.) were disappointing. Individuals who tolerated large initial doses were not benefited. However, persons who obtain a local reaction (erythema) from a test dose of 0.02 to 0.03 given intradermally, especially if such focal symptoms as sneezing, tingling and thin, watery nasal secretions are produced, are likely candidates for successful prophylaxis. Vaughn<sup>17</sup> states that his best results in vaccine therapy are obtained by vaccines which produce a wheal and uses this as a criterion of excellence of the vaccine. Might it not be that such individuals are more sensitive and hence are more likely to be benefited? After the test injection the initial dose should be reduced to 0.01 cc. and in the occasional very sensitive case to still smaller doses. Extreme sensitivity is sometimes encountered. One patient had a violent asthmatic attack within 15 minutes of an injection of 0.01 cc. and the dose had to be reduced by serial dilutions to 0.0005 cc. of the original vaccine before a local reaction was avoided. That the reaction was not due to chemical preservative was demonstrated by injection of full strength bacteria-free fluid vehicle. The injections have been given at weekly or bi-weekly intervals over a period of two years, and a dose of 0.4 cc. is now tolerated.

Vaccine has proved to be a valuable adjunct in the treatment of asthma in this individual, nor has she had acute rhinitis during this period. Dick<sup>2</sup> warned against producing asthma with respiratory vaccine, Forbes<sup>2</sup> found it of curative value in treating asthmatic bronchitis, and Walker<sup>2</sup> used it to cure asthma following colds. In another patient in whom urticaria had occurred after self-administration of oral vaccine, a local wheal about four inches in diameter was produced by 0.001 cc. Half this dose was tolerated, and she is now receiving 0.01 cc. without reaction. A patient with chronic uveitis due to chronic maxillary sinusitis is receiving a mixed autogenous and stock vaccine of the same concentration. Despite three months of treatment a dose of 0.002 cc. still produces tingling and dripping of the nose and a sense of pain and swelling at the site of the Caldwell-Luc operation. As a rule 0.01 cc. (20 million organisms) can be given without reaction. This is in line with Brown,<sup>18</sup> who recommends an initial dose of 0.1 cc. (5 million organisms) in bacterial allergy, and is a small portion of the usual initial doses found in the literature. When a dose which produced a slight erythema is tolerated without reaction the quantity should be gradually increased, at first at four to five day intervals, later at weekly intervals, and when a maximum dose of 0.2 to 0.4 cc. (which is all that can be tolerated in a really superficial intradermal injection) is reached the interval can be lengthened to two weeks or more. I wish particularly to emphasize the necessity to individualize the initial dose and the subsequent rate of increase. Given, Bunting, Gillet and Wynn (quoted by Thomson and Thomson<sup>2</sup>) concur in this opinion. For this reason, when employing autogenous vaccines, it is well to establish an initial dose from a small sample of known strength, and then request the laboratory to make up a specific dilution.

I wish to call special attention to a syndrome which I believe to be bacterial allergic rhinitis. These patients complain of nasal obstruction with thin, watery nasal secretion, with or without sneezing. The symptoms may be more or less continuous or paroxysmal with remissions. They either "have a cold all the time," or frequently think they are getting a cold which never develops beyond the so-called second (watery secretion) stage. Allergic survey fails to reveal a cause, or if specific causes are supposed to exist avoidance does not relieve the symptoms. I have been unable to demonstrate eosinophils in the nasal secretion, probably because it is so watery the cells are too infrequent to yield a good smear. If there is any seasonal variation the symptoms are apt to be worse in winter. If these patients develop an acute infectious head cold the chronic

symptoms are aggravated for a protracted period after all gross evidence of nasal infection has subsided. The nasal mucosa may be normal in color or pale and boggy. The symptoms are easily provoked by moderate doses of respiratory vaccine and are controlled by small doses. It is usually impossible to increase the dose very much even after many injections without precipitating focal symptoms, but a maintenance dose at bi-weekly intervals gives the patient relief. In 1929 Thjøtta<sup>10</sup> reported curing vasomotor rhinitis by autogenous vaccine.

In most articles the authors speak of immunization. Vaughn, however, in speaking of pollen injections uses the term hyposensitization. Nelson<sup>11</sup> employs the phrase "desensitization for the common cold." If a specific immunity were conferred the individuals so treated should be immune to pharyngeal and tracheal infections, and to staphylococcic infection such as styes and boils. In my experience they are not. The symptoms avoided are vasomotor symptoms resembling those of pollen rhinitis. Moreover, the treatment which has been effectual has been the employing of small, individualized intradermal doses as is done in pollen hay-fever. I conclude, therefore, that the benefit is from partial desensitization and that it may be specific for certain organisms. The effect, of course, may be the result of nonspecific protein therapy. Kerr<sup>1</sup> suggests that nonspecific benefit may possibly result from action on the autonomic nervous system causing relaxation of vessel spasm and thus minimizing the effect of draughts and cooling. With the very small amounts of protein used in intradermal doses this does not seem likely.

There has been much experimentation and speculation concerning the etiology of the common cold, with some evidence to support all the alleged causes. Laboratory experience implicates a filtrable virus, perhaps as an activator of bacterial virulence (Paul,<sup>20</sup> Dochez<sup>21</sup>), but contrary to known virus diseases, no immunity is conferred upon the victim. Bacteria are implicated but perhaps only in the later stage. Statistical studies emphasize a marked increase in incidence at the seasons of widest temperature fluctuation.<sup>5</sup> The negative result of Kerr's<sup>1</sup> experiment in attempting to transfer colds in humans under controlled conditions of temperature and humidity suggests that drying of the nasal mucosa or skin evaporation may be a factor. Metabolic upsets are cited as a predisposing cause, but the experience of many individuals would indicate that over-fatigue from working under pressure or dissipation is a more frequent factor. It is noteworthy that, contrary to popular belief, isolation from group contact or living in polar regions does not assure freedom



from colds. When Ellsworth was rescued after two months without outside contacts he had a cold. After a year in Little America Byrd's expedition had an outbreak of colds attributed to opening a box of clothing.<sup>1</sup> Amundsen<sup>22</sup> stated that Eskimo in the region of Hudson's Bay, without contact with more southerly natives, all experienced severe head colds lasting three weeks every spring and autumn. I would like to suggest that possibly the watery stage is in the nature of an allergic reaction predisposing to development of the final phase. Against this is the fact that a single attack of allergic rhinitis does not lead to the symptoms of the third stage of the common cold. However, the therapeutic efficacy of ephedrine *per os* (v.i.) and the presence of eosinophils in the secretion (Hansel<sup>23</sup>) tend to support this view.

Since the etiology of this far from trivial malady is not known, treatment must necessarily be empirical. A sure "cold-cure" would lead to fame and riches, and the wide variance in treatment employed is a measure of therapeutic failure. Despite this I suggest that the following procedure is frequently efficacious in aborting incipient rhinitis. Local nasal treatment does not alter the course of the disease, but shrinking the nasal mucosa with ephedrine in physiologic saline affords transient relief of obstruction and does no harm. Most of us are in agreement with Van Alyéa<sup>24</sup> that no other drug should be used in the nose. The patient is given 1/60 cc. of respiratory vaccine intradermally in the upper arm (1/20 or 0.5 cc. of vaccine which has been diluted to 1/3 the original strength, containing 33.3 million bacteria). The use of vaccines in the treatment of acute respiratory infection was recommended thirty years ago, and Thomson and Thomson<sup>2</sup> quote six authors (Sherman, Allen, Flemming, Floyd, Wynn and Davis) as having found it of definite value. The initial doses given by the first two were 332 million and 225 million organisms, respectively, presumably by subcutaneous injection. In the other arm is given one ampoule of lipin-proteid compound (2 cc.) as suggested by Mithoefer<sup>25</sup> a few years ago. The patient is then given 16 capsules containing ephedrine, papaverine and codein of each gr. 1/4 and acetylsalicylic acid gr. 5. The latter probably has no value except to fill up the capsule. As uncomplicated acute rhinitis is not accompanied by fever or malaise the antipyretic and analgesic actions are not of particular interest. I started using ephedrine by mouth because the early symptoms of a cold closely resemble those of allergic rhinitis, and was gratified to find not only symptomatic relief but that by controlling the early symptoms the later stage was avoided. Gowan<sup>26</sup> also recommends it for this pur-

pose and Van Alyea<sup>27</sup> states that it helps keep the nose open after local shrinking. The papaverine and codein are incorporated because of the benefit pointed out by Diehl.<sup>28</sup> Stengel has remarked that when large numbers of physicians employ the same empirical remedy it is probably of some value, and in using these opium alkaloids we are following the time-honored precedent of a seventeenth century English pirate, although Dr. Dover's famous pill contains only about 1/13 gr. of active alkaloids and the combination with ipecacuanha is illogical. The capsules are taken every three or four hours depending on body weight, with a double initial dose and two on retiring. This treatment is usually efficacious in the first 48 hours of incipient acute rhinitis (the earlier the better); is more efficacious if the patient can be induced to go to bed; is not of benefit after the nasal discharge becomes thick and mucopurulent (concurred in by Gowan), and is of little or no value in sore throat and chest colds. However, in the type of acute upper respiratory infection which begins with pharyngitis and tracheitis, later ascending to rhinitis, the latter phase is frequently avoided. Unpleasant symptoms occasionally occur from this medication. The stimulating effect of the ephedrine is counteracted by the sedative action of the opium alkaloids. The latter may produce nausea and vertigo in individuals with an idiosyncrasy. If this is known in advance amytal gr. 1/4 may be substituted. The constipating effect may be counteracted by a laxative or by incorporating cascarn gr. 1/4 in each capsule. Abdominal discomfort so frequently followed the use of this drug that I discontinued it. A few allergic patients experience urticaria from aspirin, in which case the capsule may be filled up by an inert substance. Systemic reactions never result from either of the injections.

It may well be asked how one is to know if a severe cold has been avoided. One cannot compile a significant statistical series showing what percentage of those about to have a bad cold failed to develop one. But the personal experience of a given individual is a useful clinical guide. When a patient states, "My colds always begin this way and I know I'm in for a bad one," it is a measure of success that within a day or two he is symptom-free.

#### CONCLUSIONS

1. In most reported series of attempted vaccine prophylaxis of the common cold no attempt was made to individualize the dosage relative to the patient's sensitivity. In many, significant data are missing.

2. Analysis of published reports fails to reveal the cause of widely divergent results.

3. Small, intradermal, individualized prophylactic doses of respiratory vaccine continued throughout the season give protection in many individuals.

4. Avoidance of rhinitis may be expected in sensitive individuals and probably is the result of partial desensitization.

5. By this method no immunity is acquired against respiratory infection other than rhinitis.

6. A clinical syndrome probably due to bacterial allergic rhinitis is described.

7. A frequently successful treatment of early acute rhinitis is outlined.

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## PSYCHOPHONASTHENIA SYNDROME\*

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For many years at our clinic we have observed a number of patients who present a voice condition which strikingly illustrates the influence of the psyche over the soma. While it simulates a legitimate somatic condition (*myasthenia laryngis*), it is in reality a psychic condition. For that reason, I term the disorder psychophenasthenia.

It is a condition which should be of particular interest to the laryngologist because of the severe laryngeal symptomatology, which leads the patient to consult the throat specialist.

The patient usually complains of a sensitiveness of the throat, a laryngeal hyperesthesia. His throat feels tight and constricted and he has uncontrollable choking sensations when attempting to speak. He also has symptoms of paresthesia—radiated pains in the head and neck, excessive dryness of the throat or mouth, or, in some instances, just the opposite—excessive secretions.

The voice is tremulous, pinched and grating, with pitch irregularities. It cracks frequently, the tone breaking suddenly to a lower key or choking off completely. The patient will often complain of a sensation, as one patient expressed it, “\* \* \* as though my throat were knotted up and my voice had somehow become entangled just below the knot and was coming to my mouth through a restricted area. It is a sort of pressure on me, and when I speak for long my vocal cords fairly ache.” In most cases the patient also has a definite phonophobia; he is actually afraid to speak.

Because of its localized manifestations, the condition heretofore has been erroneously diagnosed as phonasthenia—weak voice. Since it most frequently afflicts singers, public speakers, ministers, lawyers and others whose vocations call for a great deal of talking, it was assumed that the disorder was the result of fatigue of the

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\*Read before the annual meeting of the Eastern Section of the American Laryngological, Rhinological and Otological Society, Philadelphia, January 10, 1941.

phonatory organs. For instance, we can trace a thesis on voice fatigue as far back as 1600.<sup>1</sup>

This idea of fatigue as an etiologic factor is stressed in all the subsequent writings on the subject. In 1906 Flatau<sup>2</sup> wrote on "Die funktionelle Stimmeschwäche (Phonasthenie) der Sänger, Sprächer, und Kommandorufer" — "The Functional Voice Weakness of the Singer, Lecturer and Army Officer." A few years later Imhofer<sup>3</sup> elaborated on "Ermüdung der Stimme" — "Fatigue of the Voice." This idea of considering all such voice conditions as local laryngeal involvements still persists today.

However, in my clinical experience I have found it necessary to distinguish diagnostically and therapeutically between true phonasthenia and pseudo phonasthenia, or what I term psychophonasthenia. In the former (phonasthenia) there is always some definite local pathology. In the latter (psychophonasthenia) laryngeal findings are negative or if there is some pathology, it is so slight as to be entirely disproportionate to the severity of the voice involvement.

Such cases of phonasthenia with no apparent local pathology have been frequently described by writers on the subject. For instance, Flatau cites several examples, but, like other workers, he attributes the condition to a quantitative and qualitative misuse of the voice.

Subjective emotional symptoms have been frequently recognized in such cases, but have been assumed to be the result of the voice disorder or explicable as "phenomena of fatigue." However, observation and study of a series of cases over a period of years have led me to the conclusion that just the opposite is the case — the emotional factors are not the result of the voice condition, but the cause of it — and that the disorder is a somatic manifestation of an emotional maladjustment based on a definite psychobiologic variability of the organism. The disorder is essentially one of psychic origin, that is, the psychic conflict is basic and the voice symptom secondary; and consequently the only correct designation is psychophonasthenia.

There are certain characteristics so common to all those who present the symptom of psychophonasthenia and so frequently repeated that a definite psychophonasthenic personality may be postulated and a definite syndromic picture may be drawn.

The psychophonasthenic is a variant of the hysteric personality. He is abnormally suggestible, but unlike most of the true hysterics he is usually cultured, intelligent and well educated. On the other hand, however, he is unsocial, retiring and aloof, and tends to with-

draw from the social milieu. Investigation will reveal that this tendency to withdrawal was well marked long before the appearance of the voice symptom itself, and that the individual has always been timid, aloof and extremely sensitive.

Clinically, the psychophonasthenic demonstrates decided evidence of sympathicotonia. He displays a marked lability of the pulse and blood pressure with unusual tachycardia when under emotional stress, and a tendency toward generalized and localized fatigue. He is restless, apprehensive and usually in a constant state of nervous tension. He has an exaggerated capacity for response to stimuli and a relatively high potentiality for the spread of emotional tone, so that his mental and physical activities are continually being disturbed or inhibited because of uncontrolled reactions. In brief, the one outstanding somatic finding is marked instability in the functioning of the vegetative nervous system with special dysfunction of the vasomotor apparatus.

We do not know the exact nature of the neurologic mechanism which produces this instability of the psychophonasthenic, but evidence points to the conclusion that there is some constitutional taint present which predisposes the individual to neuroticism. From our observations we feel that it may in all probability be a hypothalamic involvement. However, this constitutional variability would not in itself cause the psychophonasthenic's severe neuroticism were it not for his early atypical environment. Nor would it cause his disabling symptom without some active precipitating factor.

Investigation will usually reveal that all of these patients were the victims of early parental neuroticism, the effects of which are evident in the repressions and inhibitions from which they all suffer. Furthermore, in most instances they come from homes in which intellectual or artistic achievement is stressed, so that the individual fails to develop a well-rounded approach to life but comes to over-value intellectual, artistic or other pursuits at the expense of his personality as a whole. Thus his emotional development is retarded and remains on an adolescent level. As the individual grows older and environmental demands become more exacting, unconscious feelings of inadequacy and inferiority assail him. Intrinsicly he doubts his ability to measure up to a necessary standard in a competitive world. An unconscious anxiety develops, which in time is converted into a physical manifestation — psychophonasthenia.

This frequently occurs in late adolescence. Adolescence is a time of crisis when the young man or young woman who has previ-

ously been a child is suddenly called upon to make adjustments to life on an adult level. At best he finds such adjustments difficult because the organism as a whole is out of balance during this pubescent period. Glandular disturbances, too, frequently contribute to the general instability. If the individual is especially sensitive and is already predisposed to neuroticism, he will be more than ordinarily affected by the changes taking place and will feel particularly inadequate to the demands which his physiologic maturity imposes upon him. If these demands are unusually exacting, he may resort to a neurotic solution of his problem. Psychophonasthenia is one such neurotic solution.

When the condition develops in later years, it can usually be traced to some crisis in the individual's personal or professional life. But no matter when the condition develops, it has its origin in a basic feeling of inferiority and in unconscious repressions and conflicts. The individual has a subconscious fear that he will not be able to meet successfully the crisis which faces him. His anxiety is physiologized in the vocal tract. He develops psychophonasthenia, and thus furnishes his ego with an excuse for the anticipated failure.

Essentially these people are introverts, but due to their higher level of intellectual development they often find themselves in vocations which call for decided extrovert attributes—the ministry, law, teaching, etc. Because of the very nature of their vocations, precipitating crises keep recurring and reinforcing their neurotic symptoms.

A few case histories from our recent research study on psychophonasthenia will illustrate these points. In each case you will note, in addition to an atypical home environment, early evidence of neuroticism in the patient, inability to cope adequately with the difficult or trying situations of life, and eventually a complete failure to adjust to some one crucial situation.

#### REPORT OF CASES

CASE 1.—E. R., a business man, aged 46, gave a history of psychophonasthenia of nine years' duration. Our anamnesis revealed an early home environment saturated with parental neuroticism. The patient as a child and young man was timid, nervous and introverted. After a brilliant school and college career, he became affiliated with a small but successful advertising agency. For several years most of his work consisted of copywriting and planning campaigns, the senior partner doing the contact work. Everything progressed well until the partner died. Naturally the patient had to assume added responsibilities, which included contacts and conferences with clients where it was frequently necessary to address a group of executives. From this time on his voice symptom gradually



developed. He visited a number of laryngologists, but laryngeal findings were always negative, as was the case when he was finally referred to us.

CASE 2.—S. W., a school teacher, aged 28, gave a history of psychophonasthenia of eight years' duration. However, she could trace distinct evidence of general neuroticism since the age of 12. The anamnesis revealed that during her pubescent period she developed a marked self-consciousness. She became timid, unsocial, retiring, and morbidly afraid of associating with the opposite sex. A college graduate at 19, she became a teacher in a rural southern school. Many of her pupils were as old as she was and she found it difficult to maintain discipline. While she continued with her teaching for the next six years, she distinctly remembers that the voice difficulty, although slight at the time, began during her first year of teaching. It became gradually worse. Threatened with the loss of her position, she began to look for relief. Although laryngeal findings were negative, she was given many forms of treatment. The throat specialist advised a voice rest, the family physician prescribed tonics, a chiropractor gave her "adjustments," but all to no avail. Her voice became worse and she lost her teaching position. Since that time she has been unable to engage in any line of endeavor which requires speech.

CASE 3.—A. L., aged 60, an engineer, suffered from psychophonasthenia for three years. The anamnesis revealed that he had been under severe strain both at home and at business, where his superior was often critical and exacting. At the time that he began to have difficulty with his voice he was in line for promotion to an executive position which would entail increased responsibilities. His voice gradually became worse and finally, when the promotion was imminent, the disorder became so serious that he took a leave of absence and came to our clinic for help.

In view of his age and the fact that the underlying conflicts were so deeply ingrained, we felt that the only way to relieve his psychic tension was to lighten the environmental pressure. He was advised to retire rather than to accept the executive position. Since his retirement there has been a gradual improvement and his voice is now almost normal.

In this case, too, laryngeal findings were negative.

CASE 4.—A. E., aged 51, a dietitian, suffered from a hoarse, strained, choked voice for four years, but laryngeal findings were negative. The anamnesis revealed that the patient had always been shy and timid and, as a child, acutely self-conscious when reciting in the classroom. She stated that since childhood she has had a strong inferiority complex. However, she completed a course in home economics and became chief dietician of a hospital, a position which she held with no difficulty for many years. About four years ago it became part of her duties to give public lectures. Shortly after the lectures began she experienced difficulty with her voice. In spite of treatment by laryngologists and voice teachers, the disorder gradually grew worse until the patient was completely incapacitated for lecture duty.

CASE 5.—E. T., housewife, aged 49, suffered from psychophonasthenia for six years. Laryngeal findings were negative except for a slight epithelial thickening at the posterior commissure. The patient gave a history of an unhappy child-

hood colored by the neuroticism of a domineering, erratic father. Symptoms of maladjustment were evident early. As a child and young woman, the patient was shy, morbidly self conscious and unsocial. The anamnesis revealed that she had been twice married and divorced and that her voice condition developed shortly after the second marriage. "My husband constantly corrected or contradicted my every statement," she told us, "so that eventually my voice seemed to fail and I kept thinking, 'I must get away from this man.'" Although the patient was subsequently divorced, her psychophonasthenia persisted and she eventually came to our clinic for treatment.

From the foregoing histories, we see that much more than the voice symptom is involved in the psychophonasthenic syndrome and that, as I said before, the condition is essentially one of psychic origin. However, since it seemingly is a throat involvement the patient, in the majority of cases, visits the laryngologist in the hope that his throat will be relieved of its weakness. The laryngologist will, in turn, frequently be led astray by the patient, who of course is anxious to legitimize his condition organically and consequently will often give a history of laryngitis, respiratory illness or vocal strain. Occasionally the patient is aided and abetted by the presence of some mild laryngeal involvement — for instance, the larynx may show a slight lack of approximation of the vocal cords, or irregular contact of the cords, or even a slight congestion. However, in most cases there is no organic involvement at all, and, as I mentioned earlier, where there is some pathology it is never sufficiently extensive to account for the severe vocal dysfunction.

Therefore, the laryngologist when he is confronted with a case of vocal dysfunction where there is no local pathology or where the organic involvement is slight, should guard against being misled by the patient or by any superficial local condition that may be present. He should recognize the fact that, basically, the condition is of psychic etiology, and in attempting treatment he should seek the co-operation of the psychiatrist.

As already mentioned, the psychophonasthenic is a variant of the hysteric personality. Yet in many ways he differs as markedly from the patient who presents the symptom of hysterical aphonia as he does from the patient who suffers from true phonasthenia (*myasthenia laryngis*).

#### TREATMENT

Since psychophonasthenia itself, that is, the voice symptom, is the culmination of a long career of neuroticism, the underlying conflicts are deeply ingrained psychically by the time the patient has cause to seek professional assistance. For that reason treatment must

extend over a considerable period, and its main goal must be the development of a more mature, more integrated personality.

We have found that both individual and group psychiatry are necessary. The first must be introduced to uncover and resolve the patient's individual conflicts. In this connection, we have discovered a practical and simple way of uncovering many of these conflicts and repressions. The psychophonasthenic is usually so reserved and so sensitive that he resents any intrusion of the therapist into his private affairs. We have found that much better results can be obtained by having the patient write out, at leisure, a series of histories; the first on his arrival, and subsequent ones at intervals as he gains insight into his condition. This does away with antagonism and with the tension that is inevitably created when the psychophonasthenic attempts to speak at great length, especially about personal matters and experiences. The physical act of writing itself serves to drain off tensions that arise from the uncovering of unpleasant memories and repressions.

In every case, however, group therapy should supplement individual treatment. As I pointed out before, the psychophonasthenic is unsocial and retiring. He is easily hurt and extremely sensitive; by social withdrawal he makes himself independent of the world and thus protects his ego from being injured by it. Group therapy is introduced to counteract these deeply ingrained withdrawal tendencies of the psychophonasthenic and to foster his better adjustment to the social environment.

Frequently, as one of the case histories illustrates, it is necessary to modify the demands of the patient's environment by insisting that he relinquish certain duties. His abnormal psychology is based on a physiologic foundation—that is, his thoughts, feelings and actions are governed by the defects and limitations of his organism—and there are certain pressures he is not equipped to withstand. The psychophonasthenic must be made to recognize his limitations and to realize that he cannot go beyond them without injury to the organism as a whole.

Although psychologic reëducation is the most important therapeutic factor in these cases, it should always be complemented by a degree of local treatment and voice training in order to correct any laryngeal abnormalities or faulty vocal habits caused by the constant misuse of the larynx. Also, we have found it advisable to introduce relaxation therapy to counteract the extreme muscular and nervous tension which all these patients demonstrate.

However, as I have pointed out, the laryngologist should definitely recognize that psychophonasthenia is primarily a personality involvement of psychic origin. He should realize the necessity for psychiatric therapy and should advise the patient accordingly. Laryngological treatment alone will never be productive of results.

#### CONCLUSION

Psychophonasthenia is a striking example of the interrelationship of the psychic and the somatic. More and more we medical men are coming to realize that we cannot isolate the body and the mind into separate and unrelated medical units. All the phases of the organism are inextricably interrelated and this interrelationship itself is constantly undergoing change in response to the demands of the milieu in which the organism finds itself.

This is especially evident under the complexities of modern life. Our escape and anxiety conditions — our psychosomatic syndromes — are continually increasing and, as I have emphasized in other papers, if he is to fulfill his obligations to his profession, the physician of the future, whether he be specialist or general practitioner, must not only treat the ills of the soma but must administer to the disturbances of the psyche as well.

61-63 IRVING PLACE.

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XIII

CHEMOTHERAPY AND SEROTHERAPY OF  
ACUTE OTITIS MEDIA

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A group of writers<sup>1</sup> from the Mayo Clinic have recently reviewed the literature and their own cases to evaluate sulfonamide therapy in the treatment of acute otitis media. It is their conclusion that adequate drug therapy has not really prevented "surgical" mastoiditis and that the 10% incidence of toxic manifestations has often made prolonged therapy impossible in critical cases. We are in complete agreement with these conclusions and have suggested<sup>2</sup> that chemotherapy should be combined with serotherapy in order to obtain prompt control of the infection within the first five days of sulfonamide administration before the onset of toxic symptoms.

In the Children's Hospital, Boston, the out-patients do not receive sulfonamides for acute otitis media, but drug therapy has been used fairly frequently in private practice. Table I records the incidence of mastoiditis in the public and private wards of this hospital. The percentile incidence is fairly constant for the public wards but the private wards show an abrupt and sustained drop beginning in 1938. We believe that this drop is due chiefly to the use of sulfonamides and warrants the continued use of drugs for the treatment of acute otitis media.

The occurrence of mastoiditis as a complication of sulfonamide-treated otitis media during the 1939-40 season led us to draw up the following program for a series of our own patients during 1940-41:

1. Early hospitalization of patients with acute otitis media in whom myringotomy seemed indicated.
2. Early myringotomy in indicated cases.
3. Aerobic and anaerobic cultures of the aural discharge.

4. Prompt administration of sulfapyridine in full dosage immediately upon entry into the hospital. Sulfanilamide was used only when the infection was known to be a hemolytic streptococcus.

5. Immune serum for patients with no antibacterial antibody and fever, pain or purulent aural discharge persisting 48 hours after starting treatment.

6. Maintenance of chemotherapy, often in reduced doses, for three weeks in all patients.

The anaerobic cultures are essential for early successful identification of hemolytic streptococci and pneumococci.<sup>3, 4, 5</sup> Chemotherapy was reserved for patients requiring myringotomy. Sulfapyridine was chosen as the ideal drug to start treatment because of its bacterial polyvalency and its superiority over sulfathiazole in the treatment of extrapulmonary hemolytic streptococcal infections. A sufficient amount of drug was given to establish blood levels of 5 to 8 mgms.% of sulfapyridine or 10 to 15 mgms.% of sulfanilamide. Antibacterial immunity tests for pneumococci were done by the Francis method<sup>6</sup> or by agglutination tests with the patient's serum. Fifty thousand units of Lederle's concentrated antipneumococcal rabbit serum seemed to be necessary for passive immunization. Anti-streptococcal immunity was tested by the phagocytic method<sup>7</sup> and immune serum was obtained from human blood.<sup>8</sup>

This report is based upon patients seen from December 1, 1940 to August 1, 1941, who had positive aural cultures of beta hemolytic streptococci or pneumococci. The first patient treated under this program was seen late in the course of the disease, received inadequate serum and progressed to mastoiditis. In the subsequent 39 cases there was no instance of "surgical" mastoiditis (Table II). It is apparent that serum was most often used for those infections known to progress most frequently to mastoid involvement, namely, the hemolytic streptococcal and Type III pneumococcal infections. It is interesting that the percentage of patients requiring serum is roughly comparable to the percentage incidence of mastoiditis reported in sulfonamide-treated otitis media.<sup>1</sup> In no instance did inadequate early therapy make it necessary to omit the drug for toxic symptoms in a patient with uncontrolled infection.

#### COMMENT

The early treatment of acute otitis media with myringotomy and sulfonamides with supplemental immune serum for those not clinically convalescent within 48 hours has effectively prevented

TABLE I

Year	PUBLIC WARDS			PRIVATE WARDS		
	No. Mastoids	Total Admissions	Incidence of Mastoid-ectomy	No. Mastoids	Total Admissions	Incidence of Mastoid-ectomy
1930	60	5158	1.16%	63	1474	4.27%
1931	77	4543	1.69%	60	1229	4.06%
1932	47	4735	0.99%	64	1107	5.78%
1933	117	4785	2.44%	78	1173	6.88%
1934	89	4457	1.99%	77	1203	6.40%
1935	106	4364	2.42%	82	1373	5.96%
1936	91	3874	2.34%	66	1426	4.62%
1937	98	3817	2.56%	66	1618	4.07%
1938	99	3829	2.58%	43	1446	2.97%
1939	105	3777	2.78%	50	1780	2.80%
1940	140	3836	3.65%	52	1927	2.69%
1941 (until July)	53	1802	2.94%	25	973	2.57%

TABLE II

ORGANISM	ACUTE OTITIS MEDIA	IMMUNE SERUM	MASTOIDECTOMY
Hem. Strep.—Group A	8	3	0
Not Groups A, B or C	1	0	0
Pneumococcus—Type I	6	0	0
Type II	1	1	0
Type III	8	6	1*
Type IV	2	0	0
Type VIII	2	1	0
Type IX	1	0	0
Type XVIII	1	0	0
Type XIX	2	2	0
Type XXIII	1	0	0
Type XXIX	1	1	0
Untyped	6	0	0
Total Pneumococcal	31	11	1
Total Pneumococcal and Streptococcal	40	14	1

\*One patient developed mastoiditis. Seen on fifth day of otitis media and received only 20,000 units of antiserum.

"surgical" mastoiditis in patients with hemolytic streptococcal or pneumococcal infections in a series of 40 patients. A larger series and experience for more than one year are necessary for the critical evaluation of these results. However, the experience with this plan of treatment encourages us to continue the regime as the one most likely to prevent surgical operations upon the mastoids in children suffering from upper respiratory tract infections.

19 BAY STATE ROAD.

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## XCIV

# A SKIN REACTION CONTROLLED LOW DOSAGE METHOD OF TREATMENT WITH STAPHYLOCOCCUS TOXOID: ITS USE IN A CERTAIN TYPE OF ACUTE RECURRENT RHINITIS

A FIVE YEAR CLINICAL STUDY OF 394 CASES

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DETROIT

*Staphylococcus toxoid* was introduced in this country in 1935 following its extensive clinical use abroad.

The toxoid was of proven value in the laboratory animal, and great interest developed in this new therapy following the remarkable clinical results obtained by Dolman<sup>1</sup> in the treatment of a variety of staphylococcic infections.

In 1933 Dolman mentioned the favorable action of the toxoid in the treatment of persons who were subject to frequent colds. In 1935 he described in detail the treatment of 23 patients having recurring upper respiratory infections. He called the infection "recurrent staphylococcic sinusitis." Pure staphylococci were usually recovered in the repeated cultures taken from the nose during the attacks. The attacks were controlled in some instances for three years.

Buchman<sup>2</sup> in 1937 after an extensive trial of the toxoid in the treatment of staphylococcic osteomyelitis could not confirm the favorable results reported by others.

Complete reviews of this subject were reported by Rigdon<sup>3</sup> in 1940 and Longacre<sup>4</sup> in 1941. The majority of the clinical reports seemed to indicate that the toxoid was not of specific value in the treatment of human staphylococcic infections.

I began using the toxoid in 1935 in the treatment of various pyogenic infections and other painful infectious symptom complexes of unknown etiology. Some persons were benefited by the treatment. Exacerbations and general reactions occurred in others.

I tried the toxoid in persons who were highly susceptible to head colds on the assumption that the toxoid might favorably affect the purulent stage of the rhinitis, reduce the length or severity of the attacks and prevent complications. Improvement occurred during the first few weeks of treatment. The attacks were controlled for indefinite periods.

When other persons with acute rhinitis were treated (who gave a history of having only one or two colds yearly) an opposite effect was noted. The acute rhinitis continued from week to week until injections of the toxoid were discontinued.

When normal persons who seldom had clinical upper respiratory infections were treated, sneezing attacks accompanied with copious mucus discharge began after several weeks. The attacks followed each injection. If the injections were continued a purulent rhinitis developed and persisted until treatment was discontinued.

Local reactions, often 7.5 cm. to 10 cm. in diameter, and general reactions occurred in persons who only occasionally had colds. Increased dosage was not tolerated in these persons, while the opposite was true of persons who had frequent head colds.

Low dosage seemed essential, and dilute toxoid (100 units per cc.) was used intracutaneously in order to determine skin sensitivity to the toxoid prior to therapy.

Skin tests were made with various dilutions of the toxoid. The size of the 24-hour skin reaction varied with the amount of dilute toxoid injected. The size of the skin reaction varied in different individuals. These reactions have been observed by others.<sup>2</sup>

A skin dose was found that would show a 24-hour skin reaction of 5 cm. or less in diameter in the majority of persons tested. This dose was .03 cc. of dilute toxoid.

Weekly increasing doses of dilute toxoid (100 units per cc.) were given intracutaneously in the forearm and similar doses of full strength toxoid (1000 units per cc.) were given subcutaneously in the upper arm, usually at the same time. The subcutaneous dose was gauged by the size of the previous weekly skin reaction. Dosage was increased as long as the skin reaction did not exceed 5 cm. in diameter. In this manner a graduated dosage controlled by a weekly skin reaction developed as shown in Table I. Weekly dosage was increased from .03 cc. to .12 cc. in adults and from .03 cc. to .20 cc. in children during the eight weeks of treatment. The total maxi-

TABLE I

## METHOD OF TREATMENT WITH STAPHYLOCOCCUS TOXOID

Weekly Injection	Intracutaneous Forearm (100 units per cc.)	Subcutaneous Upper Arm (1000 units per cc.)
1.	.03 cc. (skin test)	.03 cc.
2.	.04 cc.	.04 cc.
3.	.05 cc.	.05 cc.
4.	.06 cc.	.06 cc.
5.	.08 cc.	.08 cc.
6.	.10 cc.	.10 cc.
7.	.12 cc.	.12 cc.
8.	.12 cc.	.12 cc.

mum dose by this method was 660 units in adults and 991 units in children. This total is approximately one-fifth to one-tenth of the usual total dosage injected (3300 to 10,000 units).

Initial 24-hour skin reactions of less than 2.5 cm. in diameter were recorded as 1-plus; less than 5 cm., 2-plus; less than 7.5 cm., 3-plus; 7.5 cm. or over, 4-plus. One- and two-plus skin reactions were recorded as negative. Three- and four-plus reactions were recorded as positive. Complete negative reactions did not occur with this skin dose of toxoid but would occur if less than .03 cc. of toxoid was injected.

Persons having frequent head colds usually showed negative reactions and were benefited by treatment. Persons who seldom had colds usually showed positive reactions and were made worse by treatment.

Treatment with staphylococcus toxoid is characterized by either favorable or unfavorable results. Few persons were observed who did not show some clinical effect from treatment with the toxoid. A favorable result means rapid clinical improvement followed by recovery. An unfavorable result means clinical exacerbation or local and general reactions. A doubtful result means incomplete recovery.

During the five-year period, 1935 to 1940, over 394 persons having acute and chronic upper respiratory conditions, pyogenic infections and other infectious symptom complexes were treated with staphylococcus toxoid in an attempt to understand the above phenomena.

In an attempt to differentiate further between persons having favorable and unfavorable results, repeated cultures were taken from

the nose and throat at the height of any acute upper respiratory infection. Later these findings were checked by hospital cultures taken from the blood, urine, lesion, nose and throat of patients and personnel.

Persons having frequent afebrile head colds and negative skin reactions usually showed pure staphylococci in the repeated cultures taken from the nose. *Staphylococcus albus* predominated. [The afebrile upper respiratory infections in these persons began in the nose (ectoderm) and descended to the throat and the bronchi.]

Normal persons having infrequent febrile throat or nose colds and positive reactions usually showed streptococci, occasionally *Staphylococcus aureus* and other organisms. [The febrile upper respiratory infections in these persons usually began in the throat (entoderm) and ascended to the nose, the ear or the sinuses or descended to the larynx or the bronchi.]

From an analysis of the skin reactions, culture findings and results of treatment with staphylococcus toxoid patients appeared to be divided into two major groups:

Group I. (a) Frequent endemic afebrile head colds, (b) negative skin reactions, (c) *Staphylococcus albus* (and *aureus*) predominant, (d) tolerant to increasing doses of staphylococcus toxoid, (e) favorable results.

Group II. (a) Infrequent epidemic febrile throat or nose colds, (b) positive skin reactions, (c) occasionally *Staphylococcus aureus* (streptococci predominant), (d) intolerant to increasing doses of staphylococcus toxoid, (e) unfavorable results. (*Staphylococcus aureus* was occasionally found in the nose of Group II persons having acute febrile rhinitis.)

In 1938 a small number of Group I and Group II persons was selected and treated with the toxoid. Persons in Group I had favorable results. Persons in Group II had unfavorable results.

In 1939 staphylococcus toxoid, like typhoid vaccine and other bacterial antigens which upon introduction appeared to have specific therapeutic properties seemed well on the way to clinical discard. The specific-like results obtained by this low-dosage method seemed to indicate that the clinical failures were due to too large dosage (Wright) and improper selection of cases for treatment.

The same year a trial of using the toxoid in known or suspected hospital staphylococcic infections and other symptom complexes was

made possible by the kind cooperation of Dr. Burt R. Shurly, Detroit, Mich. and the Staff of William J. Seymour Hospital, Eloise, Mich.

Patients in the various hospital wards were skin-tested with the toxoid and 58 out of 224 persons skin-tested were given full doses of the toxoid.

Mistakes in selection occurred. Results were not so good as expected. In some persons the toxoid did not show a skin reaction 24 hours later. Complete negative reactions had never been observed during the three years of previous skin testing with .03 cc. of dilute toxoid.

Subsequent skin testing in old and new cases showed a reduction in the size of the 24-hour skin reaction. A reinterpretation of the initial skin reaction was necessary.

During the remainder of 1939 and 1940 other staphylococcus toxoids were used in an attempt to understand the changes in the skin reactions and the results of treatment. In 1940 a further decrease in the size of the skin reaction occurred with accompanying changes in treatment results, and the use of the original toxoid had to be discontinued.

Typhoid vaccine was used in comparative skin testing. The 24-hour skin reaction produced by typhoid vaccine closely resembles the skin reaction produced by staphylococcus toxoid. Typhoid vaccine like staphylococcus toxoid seems to produce opposite skin reactions to those produced by Schick and Dick test material. Negative reactions occurred in persons who were apparently susceptible to the disease. Positive reactions occurred in persons who seemed to be protected against the disease (Gay). In 1939 during an epidemic of typhoid fever, typhoid vaccine was used by this low-dosage method in the treatment of typhoid fever. The result of skin testing and treatment with the vaccine during this epidemic will be reported later.

#### MATERIAL USED

Stock commercial toxoids 1, 2 and 3 were used during the period 1935 to 1940. The results are based on the first toxoid used during the entire five-year period. This toxoid was uniform in action from 1935 to 1939. Changes occurred in 1939 and 1940. Toxoids 2 and 3 were then used for comparative purposes. All three toxoids are supplied in two strengths, dilute toxoid (100 units per cc.) and full strength toxoid (1000 units per cc.). All are manu-

TABLE II  
SKIN REACTION RESULTS

	Skin Tested	Group I Skin Reaction Negative (1 or 2 plus)	Group II Skin Reaction Positive (3 or 4 plus)	Doubtful Skin Reactions (untreated)
Total	394	246 (63%)	119 (30%)	29 (7%)
Office	170	117 (69%)	53 (31%)	
Hospital	224	129 (58%)	66 (29%)	29 (13%)
		percent	percent	number
Acute Rhinitis	160	75	25	10
Asthma	18	44	56	1
Sinusitis	31	20	80	
Otitis	18	20	80	
Empyema	5	100		
Osteomyelitis	27	87	13	2
Acne Skin Inf.	22	80	20	4
Diabetes	24	59	41	2
Myelitis	12	60	40	2
Neuritis	58	67	33	4
Arthritis	78	46	54	1

factured according to National Institute of Health standards and are approved by the A. M. A. Council of Pharmacy and Chemistry. Toxoids 4 and 5 are now being used.

#### RESULTS

Results are based on the use of the toxoid in 394 persons and on the analysis of the individual cases studied during the five-year period. Many persons were under observation during the entire period.

*Skin Testing Results.* The results of skin testing are shown in Table II. Of the 394 persons skin-tested 63% showed negative reactions and 30% showed positive reactions. The 7% of doubtful skin reactions could not be classified without a test of therapy. Of the 160 persons having acute rhinitis 75% showed negative reactions. Negative reactions occurred in 87% of the 27 persons having osteomyelitis and 80% of the 22 persons having acne, carbuncles and surgical infections. The majority of persons having neuritis, myelitis and diabetes also showed negative skin reactions.

Positive skin reactions were found in the majority of persons having arthritis, sinusitis, otitis, ulcerative cellulitis, asthma and hay fever.

A skin test dose of staphylococcus toxoid (.03 cc.) upon intracutaneous injection is painless; the reaction in 24 to 36 hours is a swollen, edematous spreading erythema of varying size, accompanied with pruritis and pain.

The skin reaction in Group I cases reaches its height in 24 hours and rapidly recedes. The skin reaction in Group II cases begins earlier, reaches its height in 36 hours and gradually recedes.

The increase in the skin reaction size upon increased dosage in Group I cases rarely exceeds 5 cm. in diameter. A later decrease in size, edema, pain, pruritis and erythema was noted. In Group II cases it was often impossible to increase the dose over .05 cc. (5 units) due to the large 4-plus skin reactions.

Changes in the results of treatment followed the changes occurring in the character of the skin reactions.

Different toxoids showed different skin reactions. Toxoid 1 was uniform in action until 1939. Stock dilute toxoid 2 often showed no 24-hour skin reaction. Stock toxoid 3 showed more immediate skin reactions which often disappeared before the 24-hour reading. The edema and erythema effects are lacking in all five toxoids. Toxoids 4 and 5 show approximately the same size skin reactions as toxoid 1.

Control skin testing with heated toxoid, buffered and physiological saline diluent rarely showed 24-hour skin reactions.

*Bacteriology.* One hundred and nine cultures were taken from the nose of office cases of acute upper respiratory infections. The findings are reported for what they are worth. The bacteriological findings as reported by local hospital and private laboratories were as follows: Pure staphylococci were found in 66% of the cultures; 38% were reported as *albus*, 10% as *aureus*, 18% as mixed or pyogenes. Other organisms found in pure or mixed cultures were reported in 44%. These included nonhemolytic and hemolytic streptococci and *Str. viridans*, diphtheroids, *B. pyocyaneus*, pneumococci, *M. catarrhalis*, *M. tetragenus*, *B. subtilis* and staphylococci.

The majority of the hospital acute staphylococcic infections were of the *aureus* type. The majority of persons having recurrent rhinitis showed *Staphylococcus albus*. The *albus* type was usually found in the nose, the *aureus* type in the throat or other lesion.

Many bacteriological reports have been made during the past five years following the air pollution studies of Pirquet and Wells.

Hallman,<sup>6</sup> Hart<sup>7</sup> and Schiebel,<sup>8</sup> Williams and Timmins,<sup>9</sup> McFarlan,<sup>10</sup> Devenish and Miles,<sup>11</sup> Gillespie and his co-workers<sup>12</sup> showed the relation of the staphylococci in the nose and the throat to the incidence of upper respiratory infection, staphylococcic osteomyelitis, surgical and skin infections. Hart<sup>7</sup> showed the high incidence of *Staphylococcus albus* and the relatively low incidence of *Staphylococcus aureus* in air pollution studies. The low incidence of *Staphylococcus aureus* corresponds to the *aureus* findings of 10% in the cultures taken from the nose during this study. Hart and Schiebel<sup>8</sup> controlled the staphylococcic surgical infections by controlling the upper respiratory infections and the air incidence of the staphylococci.

Hudson<sup>13</sup> in 1923 reported that Williams, Nevin and Gurley in 1921 found staphylococci in 84% of persons having rhinitis. Hudson found staphylococci in approximately 78% of persons having colds. Of the 192 cultures taken from these persons 76% showed *Staphylococcus albus*.

These bacterial studies show that the incidence of air-borne bacteria and the infections of the nose and throat occurring in constant staphylococcic carriers are directly related to the incidence of the clinical disease believed to be caused by the staphylococci.

Group I persons having recurrent mucopurulent rhinitis usually showed *Staphylococcus albus* in the cultures. Group II persons who occasionally had febrile rhinitis occasionally showed *Staphylococcus aureus* in the nose cultures.

Of the 394 persons 193 were treated with the toxoid. Of this number 65% had favorable results and 35% had unfavorable results as shown in Table III.

*Favorable Results.* Of the 116 cases of acute rhinitis 67% had favorable results. The majority of persons having osteomyelitis, acne and skin infections, and neuritis had favorable results. An analysis of these cases showed that the majority of the favorable results obtained with staphylococcus toxoid occurred in the Group I persons.

The attacks of recurring mucopurulent rhinitis occurring in Group I persons were controlled for a year or more. Many persons have not had a return of these attacks. They do however have one or two epidemic upper respiratory infections yearly as observed in the Group II persons. In some young persons yearly treatment with reduced dosage is necessary.



TABLE III

RESULTS OF TREATMENT IN THE DISEASES IN WHICH THE  
STAPHYLOCOCCI MAY BE IMPORTANT

	Number	Favorable percent	Unfavorable or Doubtful percent
Total	193	65	35
Office	135	64	36
Hospital	58	69	31
Acute Rhinitis	116	67	33
Asthma	10	50	50
Empyema	2	100	—
Diabetic Infections	2	100	—
Acne-Boils	13	75	25
Osteomyelitis	13	85	15
Neuritis	41	51	49
Decubitus	2	100	—
Unknown Fever	2	50	50

Group I persons had the less severe hospital staphylococcic infections. Group II persons had the infrequent severe febrile staphylococcic infections and were highly sensitive to staphylococcus toxoid. Extreme caution was necessary in the treatment of febrile or moribund persons. *Staphylococcus aureus* was often found in these persons. Several intracutaneous doses of the toxoid were given every three or four days and not more than 37 units of toxoid was given during the first 10 days. Low dosage the first two weeks was important. Rapid clinical improvement was observed within seven to fourteen days by this method without general reactions. Reduction in temperature was the first indication of improvement.

Improper selection of certain persons was made during the hospital study when changes in the size of the initial skin reaction occurred. Several febrile streptococcic infections showing *Staphylococcus aureus* were treated. A clinical accident occurred in a person having postpneumonic empyema after only 77 units of toxoid had been given. The interne said the patient "drowned in his own bronchial secretions." In one other person having cellulitis an elevation of temperature and severe diarrhea developed within the first seven days. Exacerbations followed each injection of the toxoid.

Favorable results occurred in those patients in Group I having recurring low-grade persistent rhinitis or staphylococcic infections, usually in two to six weeks with full doses of toxoid.

TABLE IV  
RESULTS OF TREATMENT AND SKIN REACTION IN  
OTHER DISEASES

	Number	Skin Reaction		Favorable percent	Unfavorable or Doubtful percent
		1- or 2- plus	3- or 4- plus		
Allergic Rhinitis	1	—	1	—	100
Hay Fever	4	1	3	25	75
Asthma	10	5	5	50	50
Chronic Sinusitis	19	2	17	11	89
Otitis Mastoid	14	3	11	25	75
Arthritis	27	9	18	33	67
Rodent Ulcer Cellulitis	2	—	2	—	100

Favorable results in Group II persons having acute febrile staphylococcic infections occurred earlier (being more objective) in seven to fourteen days after the injection of only 77 units of toxoid. General reactions were avoided and if they occurred, treatment was discontinued.

Gilchrist and Wilson<sup>11</sup> reported favorable results with the use of staphylococcus toxoid in the treatment of diabetes and diabetic infections. Similar effects were noted in this study in the treatment of 14 of 24 diabetic patients showing negative skin reactions. Treatment was started in these patients. I did not know at the time that an insulin study was being conducted in the same persons. Marked reduction of insulin requirements occurred after several weeks of treatment. I was asked to discontinue the use of the toxoid in all but two persons with severe diabetic skin infections. One person in a moribund condition had a large carbuncle of the back. Rapid healing was accompanied with a reduction of the blood sugar, and the patient progressed from diabetic coma to insulin shock before the treatment was completed. The other person no longer required insulin.

*Unfavorable Results.* Unfavorable results usually occurred in Group II persons. The majority of persons with epidemic febrile upper respiratory infections, sinusitis, otitis and allergic conditions had unfavorable results as shown in Table IV. Unfavorable results occurred in Group I persons if more than eight weeks of treatment (660 units) was given; in Group II persons, if more than 77 to 198 units was given (two to four weeks of treatment). Unfavorable signs were: Exacerbation of any existing illness, loss of weight, loss

of appetite, diarrhea, extreme nervousness, tremors, restlessness, insomnia, subcutaneous Schwartzman or cutaneous Arthus phenomenon (herpetic or seropurulent eruptions), lethargy, chilling on exposure, sneezing attacks accompanied by copious mucus discharge or recurring attacks of mucopurulent rhinitis.

Toxoids 1, 2 and 3 showed unfavorable results in Group I and Group II in 1940 and had to be discontinued. Results with the use of toxoids 4 and 5 are unknown. All five toxoids will cause unfavorable results in normal and Group II persons, given the usual amounts of toxoid.

#### COMMENT

The type of upper respiratory infection which seems to be influenced by treatment with staphylococcus toxoid is commonly called chronic sinusitis, bacterial allergic rhinitis or recurrent mucopurulent rhinitis. The incidence is highest in children (with higher basal metabolic rate) and males. The highest incidence observed was 27 attacks yearly or an average of one attack every two weeks. Stiles and Chapman<sup>15</sup> made a similar study of 395 persons having low-grade illnesses. Most of these persons had more than one disease and 96% had clinical upper respiratory infections. Of this group 52% had chronic sinusitis (nose infections) and 44% had nasopharyngitis (throat infections). Staphylococci were found in 69%, mostly in the nose. Streptococci were usually found in the throat infections. In rheumatoid arthritis staphylococci were found in 56%. A corresponding incidence was found in this study.

This upper respiratory phenomenon may be explained on an autonomic nervous system basis as discussed by Kuntz<sup>16</sup> in 1936. He believes the nasal pathology is produced by the action of the toxic products upon the autonomic nerves controlling the upper respiratory mucosa. The subclinical symptoms and the referred pains in the head, neck, back and shoulders, often associated with infections of the upper respiratory system, may be explained according to Head's theory of referred pain. Favorable effects of the treatment with staphylococcus toxoid 1 prior to 1939 were: Recovery from dryness of the nose, throat, mouth, bronchi, crusts in the nose and eyes, gastrointestinal spasms, constipation, sinus arrhythmia, staccato expiration, tachycardia, nasal obstruction (edema and swelling of the erectile tissue) sensitive to temperature changes and skin vasomotor inactivity (delayed dermatographia reaction).

The cause of the different phenomena observed in different persons with the use of staphylococcus toxoid is unknown.

*Staphylococcus albus* was most often found in children and adult carriers having low-grade recurring rhinitis, while *Staphylococcus aureus* was occasionally found in Group II persons having severe epidemic febrile infections. A similar condition seemed to exist in an epidemic of upper respiratory infections reported by Coburn and Pauli<sup>17</sup> in 1941. They found that infant carriers of nonhemolytic streptococci having recurring upper respiratory infections communicated hemolytic streptococci to adults. The febrile upper respiratory infection resulting in the exposed adults was not transmitted to other adults, and was not as infectious as the nonhemolytic streptococcal infection occurring in infant carriers. Hemolytic streptococci became nonhemolytic streptococci when transmitted to infant tissues and when grown in infant blood broth. Nonhemolytic streptococci became hemolytic streptococci when transmitted to adult tissue and when grown in adult blood broth.

The greatest difficulty in a study of the upper respiratory infections is the recognition, differentiation and interpretation of exceptional cases. A clinically similar recurring rhinitis occurred in Group II persons showing nonhemolytic streptococci and *Staphylococcus albus* in nose cultures. Epidemic and endemic (recurring) rhinitis were similar in many respects. Recurring rhinitis showing pure diphtheroids or pure *B. pyocyaneus* was encountered. Treatment with staphylococcus toxoid in these cases causes unfavorable results.

Following the changes in the typical skin reactions in 1939 low dosage would not produce the typical rapid clinical improvement or exacerbation during the first few weeks of treatment with the toxoid. Prior to 1939 Group I persons noted a subjective stimulation (or euphoria) following each injection. Group II persons noted a subjective depression and had low-grade febrile reactions or sneezing attacks following each injection.

Something seemed to be lacking in the toxoid produced after 1938. Hemolytic staphylococci are usually used in making the present commercial staphylococcus toxoids in the attempt to control the severe febrile *aureus* infections in the Group II persons who were found to be highly sensitive to staphylococcus toxoid.

If the constant carriers of the common upper respiratory organisms who have low-grade recurring upper respiratory infections could be treated and controlled, the incidence of the more severe febrile infections might be materially reduced, thus simplifying the more

difficult treatment of the Group II persons. It is generally agreed that control of the carrier controls the disease.

#### SUMMARY

During a five-year period (1935 to 1940) 394 persons having acute and chronic upper respiratory infections, pyogenic infections and other infectious symptom complexes of unknown etiology were treated with staphylococcus toxoid.

A low-dosage method of treatment was used based on skin sensitivity to staphylococcus toxoid. Total dosage of 660 units in adults and 991 units in children was approximately one-fifth to one-tenth of the usual amounts of toxoid administered (3300 to 10,000 units).

An initial intracutaneous dose of .03 cc. of dilute toxoid (100 units per cc.) was used in the selection of cases for treatment.

Of the 394 persons, 193 were treated with the toxoid. Of this number 65% had favorable results and 35% had doubtful or unfavorable results. Of the cultures taken from the nose 66% showed pure staphylococci. Of the 394 persons tested with staphylococcus toxoid 63% showed negative skin reactions.

An analysis of these cases showed that patients could be classified into two major groups, Group I having frequent afebrile colds and chronic low-grade illnesses, Group II having infrequent febrile colds and more acute illnesses.

Group I persons (*Staphylococcus albus* predominant) showing negative skin reactions had favorable results when treated with staphylococcus toxoid in full doses.

Group II persons (*Staphylococcus aureus*, streptococci predominant) showing positive skin reactions had unfavorable results when treated with staphylococcus toxoid. Fractional doses of the toxoid were often of benefit.

Persons having recurrent mucopurulent rhinitis showing staphylococci predominant in nose cultures recovered from the attacks when treated with staphylococcus toxoid. The attacks were controlled for a year or longer.

Persons who seldom had colds developed sneezing attacks and purulent rhinitis when treated with staphylococcus toxoid.

The skin reaction produced by staphylococcus toxoid was negative in persons who were constant carriers of the staphylococci and

positive in persons who were periodic carriers of the staphylococci. These skin reactions seem to be the opposite to those produced by Schick and Dick test material. Similar opposite skin reactions were observed with the use of typhoid vaccine (Gay).

Staphylococcus toxoid in low dosage (660 to 991 units) produced favorable results in Group I persons and unfavorable results in Group II persons.

Changes in the skin reactions and results of treatment with staphylococcus toxoid occurred in 1939. The use of toxoids 1, 2 and 3 have been discontinued. The clinical value of toxoids 4 and 5 is unknown.

The rules governing the use of staphylococcus toxoid in this study were:

1. Take cultures only in the presence of the disease process. (Organisms in pure culture are considered to be pathogenic until proven to be nonpathogenic in humans.)
2. Determine the type of staphylococci present.
3. Determine skin sensitivity to the toxoid prior to treatment.
4. Treat only persons showing negative 24-hour skin reaction.
5. Do not treat *Staphylococcus aureus* infections with full doses of toxoid.
6. Search for a primary infection when *Staphylococcus aureus* is found.
7. Treat only primary staphylococcic pyogenic infections. Remember that the staphylococci are often secondary invaders causing pus in streptococcic and pneumococcic infections.
8. Note that persons having other primary coccal infections are often highly sensitive to staphylococcus toxoid. Treatment with the toxoid will cause clinical exacerbations and occasionally clinical accidents.

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XCV

AN EXPERIMENTAL AND CLINICAL STUDY OF  
THE COMMON COLD\*

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Thermo-electric studies of the temperature of the mucous membrane as an index of vascular changes showed that rapid cooling of most cutaneous surfaces produces a reflex vasoconstriction and ischemia leading to a lowered mucous membrane temperature in the upper respiratory tract. Alterations in the temperature of the upper respiratory mucosa was found to be due to a change in the vasomotor tone of the vessels supplying these membranes. A fall in temperature indicated a vasoconstriction, a rise, a vasodilatation.

In the preceding studies of this subject<sup>1,2</sup> complete method and bibliography were recorded and hence will here be given summarily. This paper, in particular, will record the effect of emotional stress on the mucosa of the upper respiratory tract.

A thermopile was employed to measure the temperature of the nasal mucosa in the experiments conducted. The electrode was applied with constant pressure to the mucosa of the nose and the electromotive force measured through a potentiometer. Various nasal membrane sites were studied. The mucosa over the anterior third of the inferior turbinate was chosen for routine examination because this surface gave regular and dependable readings. The nasal thermopile was attached to a specially constructed head gear and electrode holder to which was fitted a micrometer. The thermopile terminals were thereby fixed upon the site to be studied so that they would remain unchanged in their position under constant and moderate pressure, and covered an area so small as not to interfere with the rise

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Presented before the American Laryngological Association, Atlantic City, N. J., Thursday, May 29, 1941.



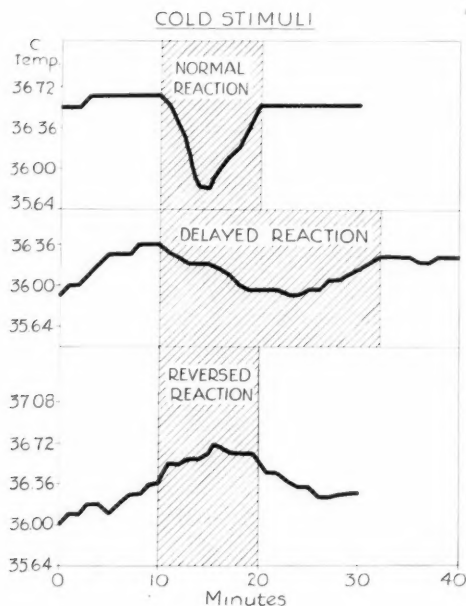
and fall of temperature in the surface under them, in response to changing vasomotor conditions. The cold stimulant, in the form of an aluminum cup, 12 cm. in diameter filled with chipped ice, was applied to the skin of the upper dorsal region. This site was chosen after an extensive study of various skin areas and found to be most uniformly sensitive for this particular stimulation. The ice-filled cup gave a surface skin temperature of  $12.6^{\circ}$  C. within the minute.

The subjects studied and previously reported upon<sup>2</sup> were nine healthy men observed for the normal vasomotor response throughout the four seasons of the year, and 54 patients for abnormal reactions. Ten subjects were observed because of their irregular reactions, caused by emotional stress and its effect on the mucosa of the upper respiratory tract and make the especial subject of this paper. All the patients in the purview of these experiments were physically and mentally normal. They each were given physical and laboratory tests, including X-ray of the chest and sinuses and were found to be free of pathology, except for a long history of infectious head colds.

The findings were as follows (also see graph):

1. *Normal Reactions to a Cold Stimulus.* There is a prompt lowering of the temperature in the nasal mucosa immediately upon application of a cold stimulus to the skin and a gradual recovery or return to the initial temperature level even while the stimulus is still being applied. The time of the return to the initial temperature varies with the temperature of the cold stimulus and the amount of skin surface stimulated. A 12 cm. pan filled with chipped ice applied to the upper dorsal region required about ten minutes to complete the vasomotor reaction. The wearing-off of the effect when a cold stimulus is maintained indicates end organ fatigue or adaptation. It has been proven to be of peripheral and not central origin, since the application of a cold stimulus to a second area, after the first effect wears off, shows a new response comparable to the initial reflex.

2. *Abnormal Reactions.* Just prior to, during and following a head cold there is a period of vasomotor suspense, i. e., a cold stimulus applied to the cutaneous surface produces no vasomotor response in the mucous membrane. This suspense of the vasomotor reaction is due to local changes within the mucosa, produced, presumably, by the toxic products of the infection upon the vasomotor endings. In the interim between head colds, the very frequently infectious head cold case presents a very much delayed reaction to a cold stimulus,



Graph 1.

i. e., while in normal cases the reaction to a circumscribed cold stimulus is completed in 10 minutes, in the infectious case the reaction time is 20 minutes and frequently longer. In some cases the mucous membrane temperature, in such instances, remains depressed after cold stimulation for several hours.

3. *Irregular Reactions.* These manifest themselves as follows: (a) a much delayed reaction; (b) a reversal of the normal response, i. e., the cold stimulus produces a rise instead of a fall in the temperature of the mucous membrane. Irregular reactions to cold stimuli were found in two types of cases, in the normal and in the infectious head cold. In both, emotional stress affected the reactions. If the emotional strain was sudden and severe the vasomotor response was reversed, and if it was prolonged, the reaction was delayed.

Each graph represents the mean curve of the number of subjects studied. Particular attention is called to the sharp outlines of the normal reactive period in contrast with the uneven contours of

the delayed and the reversed reactions. It is also noteworthy that a normal subject will present, under emotional stress, an irregular curve in both the reversed and the delayed reactions. The sharp lines seen in the curve for the normal reactions become uneven under emotional stress.

Every patient was studied for a period of three weeks prior to the administration of treatment, i.e., he was examined on an average of five times weekly to determine his particular average vasomotor response to a cold stimulus. After treatment was instituted, the subject was studied two to three times weekly. The treatment consisted of:

1. Mental and environmental adjustment, especially emotional equanimity through self-control.

2. Vasomotor massage applied in the form of hydrotherapy, i. e., hot and cold water showers. This treatment was given on the assumption that the common cold starts with a disturbance of the heat-regulating mechanism of the body, i.e., the inability of the nasal lining membrane temperature to return rapidly to normal after the body had been chilled. It was found that the better the functioning of the heat-regulating center of the body, the more responsive are the blood vessels of the nose to cold stimuli and the less the tendency to infection. It seemed, therefore, that the prevention of the onset of the common cold might best be achieved by training and developing the auxiliaries of the heat-regulating center to respond quickly to altered temperature conditions.

3. A low-starch diet, and especially were wheat cereals eliminated; also included were moderate amounts of proteins and quantities of fruits and raw vegetable salads. It was apparent that the lack of a well-balanced diet and vitamins caused a predisposition to colds. A diet rich in fresh fruits, raw vegetables, dairy products, moderate amounts of meat and fish, low starch composition, provides a balanced diet and sufficient vitamin content. All cereal foods and meats are acid producers, while fruits, vegetables, and milk products maintain the body's alkaline needs. The blood normally keeps balanced on the slightly alkaline side.

#### REPORT OF CASES

CASE 1.—G. A. T., a bank teller, 34 years of age, presented a history of numerous infectious head colds for the past two and one-half years while before he had had only one cold yearly. He had acquired the position he now held after working in the bank in less

remunerative capacities. Shortly after he was advanced to his present post, about two and a half years ago, he developed a succession of head colds. He liked his work but he was worried continually lest he lose his job, since the bank's rule was that two errors made by a teller meant his dismissal. A vasomotor study of the patient's nasal mucous membrane showed a much delayed reaction to a cold stimulus. He was placed under treatment and given further study. No improvement was seen after 12 months and the vasomotor reactions continued to be delayed. His colds were frequent and more severe—he had seven colds during this period and lost with each an average of a week from work. He was advised to change his place of employment and seek some other occupation, since his anxiety, fear and worry were affecting his health. He followed this advice and became a salesman for an automobile accessory company. After the change and while still under treatment, he did not show improvement in the nasal mucous membrane reaction in subsequent study until he had become acclimated to his new job and found it steady and to his liking. He was shortly earning what he was paid as a teller and thereafter his vasomotor reactions showed noticeable improvement. In the second year of treatment and observation, he had three colds, the first two severe, the third mild. Further vasomotor study showed gradual improvement towards normal. In the third year, with continued treatment, the patient had two mild colds, and gave normal reactions in the majority of days.

CASE 2.—C. T. W., a male, 37 years old, sales manager for an automobile truck company, reported that for the past seven years he had had frequent and severe colds yearly; prior to this time, he recalled having two mild colds a year. A vasomotor study of his nasal mucosa showed very delayed reactions to cold stimuli. In the first year, after treatment, his colds were reduced to three, the first severe, the last two mild; his vasomotor reactions returned gradually towards the normal. In the second year of treatment he had two mild colds, and a vasomotor study showed normal reactions for the majority of days. On July 1st of the second year's treatment, the patient lost employment because the firm for which he worked became bankrupt. On August 4th of that year he had his severest cold, which kept him at home for two weeks. This was his first infectious summer cold. From June 14th, when he first learned that his firm was closing doors, until his August cold his vasomotor reactions were again much delayed. He continued his treatment diligently. From August 4th, the time of the summer cold, until he found lucrative employment in March, he averaged one severe cold

every six weeks. The vasomotor findings during this time showed very delayed reactions. In the succeeding seven months he had two colds, the first severe and the second very mild. His vasomotor reactions in this interim gradually returned to normal, and in the last four months they were normal in a majority of days.

CASE 3.—M. A., a machinist, 29 years of age, gave a history of frequent colds yearly for the past five years. A vasomotor study showed very delayed reactions. After four months of treatment these gradually returned to normal and continued thus for five successive weeks. During these five months and a week he had two very mild colds. Following the normal reactive period and while still under treatment, he developed a succession of delayed reactions to cold stimuli and then a very severe cold which kept him home for 10 days. Upon inquiry he disclosed that he had lost his job a week before his last cold. He was very worried because he had a wife with child, and two young children dependent upon him. Five weeks after his last cold he developed another, which, he stated, was the worst in several years. His vasomotor reactions continued to show delayed responses even though he continued under treatment. Three weeks after the last cold he obtained a job and his reactions returned slowly to normal. In the second year he had three colds, each less severe and of shorter duration; and in the third year with treatment, the majority of the vasomotor studies showed normal reactions and he was inconvenienced by only two very mild colds.

CASE 4.—G. M. M., a female, 11 years old, presented a history of frequent head colds for the past three years. A vasomotor study showed very delayed reactions to cold stimuli. Under treatment, and with the complete cooperation of her mother, she nevertheless completed the year with six infectious colds, including one in July. Between colds the vasomotor observations showed similar delayed reactions. Further inquiry into the case showed that until she was six, the patient, an only child, enjoyed a normal home life in a comfortable environment. Her father died then and the mother remarried. The stepfather caused her grave irritation which had become progressively worse in the last three years. Since there were no other findings, the mother was persuaded to send the patient to her sister's home, only 30 miles away, in a similar climatic environment, for care and schooling. Treatment was continued and the vasomotor reactions observed twice weekly for the next two years. The patient completed the second year of treatment with two very mild colds and a severe one which occurred during the Christmas

recess, while she was visiting her parents. Up to this period, the vasomotor reactions were less delayed and improved progressively until they reached normal. In the third year, treatment continuing, the patient had two very mild colds and gave normal vasomotor reactions in between times. At the Christmas vacation of the third year, the child was allowed to spend only one day with her parents and then returned to her aunt. She had no cold during this holiday. At the end of the third year, the mother, believing her child cured, brought her back home. In the year following the patient had four severe colds from September to June and one in July, even though her mother continued to follow the treatment prescribed. The vasomotor study was not continued into the fourth year.

CASE 5.—H. L., a school teacher, 28 years old, presented a history of frequent head colds. She was normal, slightly overweight and unmarried. A vasomotor study of her nasal mucosa showed very delayed reactions to cold stimuli. Placed under treatment she improved progressively and her vasomotor reactions became less delayed. She continued, however, to have her regular colds which became less severe and of shorter duration. She was advised to give closer attention to the treatment and to abstain from a too active social life, using most of her leisure time for rest. In the second year of treatment the number of colds were reduced to three of lesser severity and duration. The vasomotor responses to cold stimuli during the first part of the second year's treatment became less delayed, improving progressively to normal in the last two months of the year. However, in July, after several normal months, the patient developed a very severe cold which kept her home for 10 days. She disclosed that she had been engaged to be married but had suddenly decided to break the engagement. The vasomotor reactions studied were decidedly delayed and continued in this way until she developed another severe cold in September, six weeks after the last one. Treatment followed into the third year but brought no improvement; instead the patient had seven colds. Her vasomotor reactions throughout this year were very delayed.

CASE 6.—W. T. S., a bookkeeper, 27 years of age, complained of having many colds each year, increasing in frequency and severity in the past 10 years. A vasomotor study of his nasal mucosa showed very delayed reactions to cold stimuli, the most delayed of the entire group studied; a cold stimulus depressed his nasal mucosa temperature and held it depressed for well over 20 minutes, twice the length of time required for a normal reaction. The frequency and severity of the patient's colds during 12 successive months of

treatment and observation remained the same, nor did the vasomotor reactions change. This past year he had seven colds and each kept him home for a week to 10 days. The patient's history showed that he was married and had four children. He had been employed continuously for the past 15 years; he liked his work and was rendering acceptable service. He liked his children, but his wife was a nag who made life unbearable for him. Unless he could adjust his home conditions and remove the emotional distress they were causing him, he was told, no treatment would avail him. He attempted to make every adjustment and treatment was continued another year. The next 12 months brought him no improvement. He explained that he had sought his wife's cooperation but conditions at home were no better.

CASE 7.—S. M. I., a normal male subject, 24 years old, while playing cards after breakfast one morning, was found cheating. He was downed and beaten by another player. An examination, conducted in the routine manner on this subject, showed a complete reversal of the normal response, i. e., a cold stimulus produced a rise in the mucous membrane temperature instead of a fall, although the subject had for many months previously given normal reactions to such stimuli. Repeated study at different times that morning and afternoon produced similar reactions. The following morning brought some change — a cold stimulus produced a delayed reaction. Not until the third day after the bout was the patient's response to cold stimulus normal.

CASE 8.—M. J., a normal subject, male, 26 years of age. While making routine examination of this subject one morning, he was suddenly frightened by a vicious dog that had broken loose from the operating room, located on the animal floor adjoining our room, and entered our laboratory. Before this happened, the subject gave normal vasomotor reactions to the cold stimuli he was receiving on different skin areas; after the incident the reactions were reversed and remained unchanged throughout the morning, returning to normal on the following and succeeding days.

CASE 9.—C. N., a normal male, 21 years old, while being prepared for examination received a telegram that his sister was in an automobile accident and had been severely injured. The vasomotor study which followed showed a reversal of the normal response to a cold stimulus, although he had previously given normal reactions to cold stimuli over a year period. His reactions remained un-

changed for the remainder of the morning. They were not studied the following morning because he left the city that day. After his return, 10 days later, his reactions were again normal.

Besides these cases nine normal men were studied. Frequently on Monday mornings their vasomotor reactions to cold stimuli were delayed although they were normal on days following. Inquiry revealed that when the subjects showed delayed reactions they had spent the week-end in carousing and sexual indulgences.

#### DISCUSSION

Very delayed reactions indicate a sluggish vasomotor state due either to environmental or emotional factors.

Poor vasomotor response of the nasal mucosa to a cutaneous cold stimulus in infectious cases is perhaps responsible for infections. A nasal mucous membrane, for a prolonged period in a state of ischemia, when present in the environment of an infectious process may become infected because of its lowered resistance during its ischemic state.

The individual suffering from repeated colds between September and June has an altered vasomotor response to thermal stimuli. This represents a maladjustment of the peripheral capillary response. So long as this abnormal reaction exists the host is susceptible to the common cold virus and the bacterial flora residing in his upper respiratory tract.

The reversed reaction found in severe emotional states, i. e., a cold stimulus applied to the skin producing a rise in the mucous membrane temperature instead of a fall, has received sundry explanations but the following seems most feasible: During emotional excitation the sympathetico-adrenal system constricts all vessels, including those of the nasal mucosa, except possibly the coronary vessels of the heart.<sup>3</sup> Cannon's studies have irrefutably shown that this system is excited under emotional stress.<sup>4</sup> During normal stimulation the sympathetic reaction overshadows the parasympathetic response.<sup>5</sup> The parasympathetic is responsible for vasodilatation in severe emotional states such as fright, in which instance it supercedes the sympathetic. Vasodilatation of the nasal vessels under parasympathetic excitation implies a rise in the nasal mucous membrane temperature. A cold stimulus then applied to the skin will produce a rise in the temperature of the nasal mucosa as the vessels cannot



be constricted to produce a normal drop because the parasympathetic overshadows the action of the sympathetic. The temperature can only go up since the vessels are already dilated by the parasympathetic phase of the excitation. This may, assumedly, account for the reversal of the normal response to a cold stimulus in severe emotional states.

The delayed reaction may be explained as follows: In patients suffering from chronic fears, worries, and "being just continuously upset," the sympathetico-adrenal system is already overstimulated and the vessels are chronically constricted. Then, if the skin is stimulated by cold, the nasal vessels constrict only partially, not as deeply as in normal conditions, just as, for example, when stimulated muscle nerve preparation is again excited, the response is weaker in contrast to the initial stimulation and a slow reaction follows after the stimulus is removed. The vessels of the nose are under sympathetico-adrenal stimulation (produced by the emotions) and if then the vessels are further excited by the application of cold to the skin, the result is a slow, sluggish delayed response with a slow recovery, just as in the muscle nerve preparation which receives added stimulation.

The repeated infectious common cold sufferer is out of adjustment with his environmental factors and therefore requires corrective aids to assist in adjustment or adaptation in the form of vasomotor stimulation (hydrotherapy), dietary restrictions, and proper mental hygienic control. Alterations in either the physical, meteorological, nutritional or emotional (mental) environment cause a common cold.

#### CONCLUSIONS

The normal subject easily unbalances his vasomotor equilibrium by severe emotional strain.

The repeated infectious head cold without any emotional background, caused only by a maladjusted environment, is markedly affected by the treatment outlined. If, in addition to the unadjusted milieu (environmental maladjustment) an emotional factor is present, the correction of the condition is not made, no matter what therapies are applied, until the emotional stress is removed.

A delayed reaction indicates a sluggish vasomotor state created either by an environmental factor or an emotional state.

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## XCVI

(FROM A GROUP OF CASE RECORDS COLLECTED AND ABSTRACTED  
UNDER THE TITLE OF "MY MOST INTERESTING CASE,"

BY NOAH D. FABRICANT, M.D., CHICAGO)

### AN UNUSUAL CASE OF RETROPHARYNGEAL ABSCESS

SAMUEL IGLAUER, M.D.

CINCINNATI

This case is of interest, not so much because of its rarity as because of the numerous complications and the fortunate concatenation of circumstances to which the patient owed her life. On January 13, 1935 a four year old girl was admitted to the Children's Hospital. On the preceding day she had become ill with chill, fever, headache, and pain over the right mastoid region and over the right side of the neck. On admission the temperature was 102 degrees, the pulse, 120, and the respirations, 26. The pharynx was markedly congested, and a postnasal discharge was present. The right drum membrane was injected, and there was evidence of right cervical adenitis. Some dullness existed over the apex of the right lung. Other findings were essentially negative. The blood showed hemoglobin, 13.2 grams; red cells, 4,980,000; white cells, 28,500; and polymorphonuclears, 84%. The urine was negative.

On the day after admission Dr. Gerson Lowenthal, one of the attending staff, made a diagnosis of right retropharyngeal swelling (abscess). This was confirmed by a roentgenogram: "Films of the cervical region show the pharynx and trachea definitely displaced forward, most likely a retropharyngeal abscess." (Fig. 1.) The next day a superficial incision through the mucosa was made over the swelling, and considerable slightly brownish pus was obtained upon spreading the incision with a hemostat. The tissues were friable.

On each of the three succeeding days the abscess was again spread with a hemostat. Shortly after the last divulsion of the abscess a rather profuse hemorrhage (6-10 oz.) ensued. The patient was taken to the operating room, ether was administered, and the bleeding ceased after pressure had been applied to the wound. Early the following day the nurse recorded "the child expectorated a



Fig. 1. Marked swelling of the retropharyngeal tissue.

medium amount of bright red blood-clots." The patient became very restless and apprehensive. Within a few hours another hemorrhage occurred followed by the expectoration of a large quantity of bright red blood. At this time I decided that ligation of the common carotid artery was imperative.

While the patient was being etherized another severe hemorrhage occurred and the child ceased breathing, for the blood evidently had entered the trachea. I immediately performed tracheotomy and introduced a suction catheter through which the aspirated blood was pumped from the trachea and larynx. Under artificial respiration and the stimulus of forceful stretching of the rectum, respiration returned. Within a few minutes another gush of blood occurred, but this was controlled by compressing the carotid against the transverse processes of the spine. While I maintained the digital pressure Dr. Henry Goodyear skillfully exposed the common carotid below my finger and ligated the vessel (infiltration anesthesia).

There was marked shock after the operation. Continuous intravenous glucose and three blood transfusions were instituted. There was no further bleeding, and no signs of hemiplegia developed. Sev-



Fig. 2. The patient after healing of the incisions.

eral hours after the ligation the red blood cells numbered 1,860,000. The tracheal cannula was removed within three days. Convalescence was slow; the patient was discharged five weeks later, at which time the red blood cells numbered 3,820,000.

It is generally conceded that the ordinary simple retropharyngeal abscess takes its origin from the breaking down of an infected retropharyngeal lymph gland. The internal carotid artery is in very intimate anatomic relation with this gland and with the peripharyngeal space in which, as explained elsewhere, I believe the abscess is usually confined. For this reason I prefer the term "peripharyngeal" abscess. Strange as it may seem, despite the close proximity of the artery to the infected area, hemorrhage seldom occurs as a complication of the abscess.

The treatment of hemorrhage complicating a retropharyngeal abscess demands serious consideration. Bleeding may occur as a single massive hemorrhage, may appear in repeated attacks (as in the case reported) or in the form of a false aneurysm. Severe bleeding or repeated bleeding should serve as a warning of impending danger and should never be ignored. Many patients have succumbed because the warning was not heeded. Ligation of the common carotid artery is indicated since it offers a practically certain method of control and should be carried out despite the rather remote possibility of hemiplegia. A possible alternative is to place a provisional protruding ligature, keeping a trained person constantly at the bedside, prepared to tie the artery at a moment's notice.

707 RACE ST.

HIGHLY MALIGNANT CARCINOMA OF THE NASO-  
PHARYNX WITH BILATERAL CERVICAL  
METASTASIS IN A CHILD — WELL  
AFTER TEN YEARS

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ROCHESTER, MINN.

A boy, 11 years of age, came to the Mayo Clinic on June 21, 1928 because of carache and a lump high in either side of the neck. The cervical masses had progressively increased in size since they first had been noticed about six months previously. The condition had been thought to be tuberculous adenitis, and an iodine ointment had been applied. In addition, tonsillectomy had been carried out three months prior to the patient's registration.

Examination revealed a hard, irregular, fixed mass about 4 cm. in diameter in either upper cervical region, just below the auricle. Also there were numerous smaller nodules of the same consistency extending to the base of the neck and into the supraclavicular region on both sides. A vascular, ulcerated mass filled the upper portion of the nasopharynx and obstructed both choanæ. Clinically, this appeared to be a highly malignant neoplasm, although the patient did not complain of the deep-seated, boring pain so characteristic of such lesions in this situation, nor was there evidence of involvement of any of the cranial nerves. General physical examination otherwise gave essentially negative results.

Leucocytes numbered 14,600, 78% of which were neutrophils, but other laboratory studies, including urinalysis, von Pirquet and Mantoux tests, and roentgenograms of the thorax, gave negative results.

Tissue removed from the nasopharyngeal mass for microscopic examination proved to be squamous-cell epithelioma, Grade IV. Biopsy of the cervical nodes was not made but clinically these appeared definitely to have undergone malignant change, and a diagnosis of epithelioma of the nasopharynx, with bilateral cervical metastasis, was made. Irradiation with radium was advised although a probable poor prognosis was given.



Fig. 1. Actinodermatitis on both sides of neck resulting from radium therapy for carcinoma of nasopharynx with bilateral cervical metastasis.

Surface packs of radium were applied over both sides of the face and neck, using 2 mm. of lead and 1.5 mm. of monel metal screening and a block of wood 2.5 cm. in thickness to secure distance. A total of 15,022 mg. hours of irradiation was administered. Radium tubes on a pliable applicator also were placed directly in contact with the tumor in the nasopharynx. Subsequently, at intervals of from six weeks to nine months, treatment with surface radium packs was repeated on four occasions in doses ranging from approximately a half to two-thirds of that of the original application, but further treatment of the nasopharynx was not given.

On returning for observation six weeks following the primary irradiation the patient had gained 11 pounds (5 kg.) and the father stated that the boy never had appeared to be in better general health. The nasopharynx was entirely free from neoplasm but multiple small nodes were still present in both sides of the neck. These nodes disappeared completely following further radium therapy.

On August 31, 1938, a little more than ten years following the primary visit, the patient returned to the Clinic for consideration of an area of actinodermatitis that had developed on either side of the neck (Fig. 1). He was in excellent general health, the nasopharynx was negative except for scarring, and only very small, apparently fibrous, cervical nodes were palpable. In the area of actinodermatitis of the neck, which obviously had resulted from the intensive irradiation, there was rather marked thickening but there was no evidence of malignant change, and replacement with full-thickness skin grafts was advised. This procedure was carried out under intratracheal anesthesia on September 3, 1938. Microscopic-



Fig. 2. Full-thickness skin graft on both sides of neck replacing area of actinodermatitis. Photographs were made a few days following removal of sutures.

ally, the tissue removed from the neck revealed the changes of actinodermatitis, with marked subepithelial fibrosis only. The skin grafts healed perfectly, and the patient was dismissed approximately three weeks later. Although he has not been heard from since, it seems safe to assume that he has had no further trouble (Fig. 2).

#### COMMENT

This case is of outstanding interest because of the unusually satisfactory result following treatment of the extensive, highly malignant carcinoma of the nasopharynx, with bilateral cervical metastasis. Tumors of such activity in this situation, and especially if the patient is young, with few exceptions produce a fatal termination in from a few months to two or three years. Other features of interest are the extent of the malignant process in the nasopharynx, without evidence of neurologic involvement, and secondary changes in the neck from irradiation.

MAYO CLINIC.



## MASSIVE HEMORRHAGE FROM THE CAROTID ARTERY

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Few pathological conditions in the pharynx entail more risk for the patient or greater anxiety for the laryngologist than massive hemorrhage from the internal carotid artery. The close proximity of this large vessel, its caliber undiminished by any branches given off as it ascends to the base of the skull, makes it particularly vulnerable to adjacent pharyngeal infection. Such infection reaches the carotid wall by extension from a parapharyngeal or retropharyngeal abscess and may so damage the vessel wall as to weaken its protective coat, which, slowly distending, forms a pseudo-aneurysm which may suddenly rupture with often devastating hemorrhage. Such hemorrhage may be so unexpected and voluminous as to allow no time for any surgical measures which might prevent the rapid demise of the patient. Fortunately, there is more often a cessation of the immediate hemorrhage as blood pressure temporarily falls, with subsequent recurrence at some later predictable moment.

Numerous reports, particularly the exhaustive study of Salinger and Pearlman, have clearly shown the folly of neglecting the warning of such preliminary hemorrhage and the wisdom of applying appropriate and courageous methods for its control. Carotid ligation has been demonstrated convincingly to be the only procedure worthy of consideration. The following case clearly exemplifies the principles involved in hemorrhage secondary to retropharyngeal abscess and serves as a text for certain observations and conclusions.

A four year old boy was admitted to the Children's Hospital in Boston on April 20, 1935 because of bleeding from the nose and throat. Four brothers and sisters were living and well, and the family history gave no evidence of tendency to bleeding. The child was born at full term, had a normal feeding history, and no previous illnesses except chicken pox. Tonsillectomy and adenoidectomy, performed nine months before, were not attended by unusual bleeding.

Two weeks prior to admission the child had a mild cold which was followed by a slight nasal hemorrhage of short duration. The hemorrhage recurred five days later and was repeated again within

two days; each time it amounted to two or three ounces and subsided spontaneously. At this time there was some swelling on the left side of the neck as well as a slight swelling on the right side of the neck. On the day of admission, April 19th, the patient had a new profuse hemorrhage from the nose and throat and vomited a large amount of old and fresh blood. At 1:30 a. m. of that day a second profuse hemorrhage could not be controlled by the family physician by means of nasal packing but was checked by the insertion of a postnasal plug. The previous day there had been some bleeding from the left ear. For three or four days prior to admission the patient had complained of mild headache, and there had been a temperature elevation up to 103° F.

Upon examination the patient appeared generally well-developed and nourished but irritable and restless. The right tympanic membrane was red, bulging, and the landmarks were obliterated. The left drum membrane was normal, the auditory canal contained masses of cheesy material, and there was a peculiar wart-like excrescence on the anterior canal wall. The nose showed a small crust of blood on the anterior portion of the septum, the throat mucosa was pale, and there was no evidence of bleeding in the nasopharynx and no gross lesion suggesting nasopharyngeal infection. An enlarged cervical gland was discernible on the left side of the neck, and a moderately enlarged gland on the right side. The skin was pale, moist and clammy. The blood count was: hemoglobin 30%, red blood cells 2,200,000, white blood cells 35,000, polymorphonuclears 92%, lymphocytes 6%, mononuclears 2%. The bleeding time was two and a half minutes, and the clotting time three minutes. The roentgenogram showed diffuse swelling of the retropharyngeal tissues but nothing to indicate localized abscess. Upon admission the patient was treated for shock. Three hours later he had a profuse hemorrhage from the mouth. His temperature rose from 101° to 102°, and upon receiving 400 cc. of glucose intravenously he had several generalized left-sided convulsions. He was given a transfusion of 165 cc. of citrated blood. During the night a dram of dark blood exuded from the left ear, apparently from the wart-like mass. His temperature was normal the next day, and he appeared better. Another transfusion was given and the right tympanic membrane incised. That night the patient had another profuse hemorrhage from the left ear, nose and throat. Treatment for shock was instituted, the ear packed, and a third transfusion given. The next day, April 22nd, following a third severe hemorrhage an ulcerated area on the left lateral wall of the nasopharynx above the soft palate was detected for the first time. It had previously been invisible to direct

inspection. Diagnosis of a retropharyngeal abscess and erosion of an internal carotid artery was promptly made and treated by immediate ligation of the common carotid artery.

The operation was performed on April 23rd under ether and avertin anesthesia. A common carotid artery ligation was done. Following this procedure the patient was apathetic. The fifth and sixth transfusions were given on April 24th. After several days of improvement a sudden severe hemorrhage occurred on April 30th with a loss of 250 cc. of blood. On this day he was given an additional transfusion, but on the following day he had another severe hemorrhage. On May 3rd he was subjected to a secondary ligation of the internal and external carotid arteries. The wound was left wide open, and the patient received an eighth blood transfusion.

The next few days the patient appeared bright and happy. On May 14th the swelling on the right side of the neck became definitely fluctuant and it was incised. The culture was hemolytic streptococcus. He improved until May 24th at which time the temperature rose to 104°, and there were definite signs of right acute mastoiditis. A simple mastoidectomy was done. Although the temperature immediately rose to 106.2° it subsided to normal on the next day. After an uneventful convalescence the temperature rose to 104° on June 3rd. This was due to reinfection of the cervical wound incident to drainage of the cervical abscess. On June 5th the patient received his ninth and final blood transfusion. On June 22nd he was dismissed from the hospital.

A first consideration of the history might easily lead to the conclusion that an unwarranted delay had occurred between the time of admission and that of ligation of the carotid. In retrospect, three previous severe hemorrhages should have made the diagnosis of carotid bleeding almost certain. However, no source of bleeding was discovered at first because the point of rupture was found to lie so high above the level of the soft palate as to escape detection. This fact emphasizes once again the importance of a most careful search for the source of the lesion.

The second interesting fact is the severe hemorrhage from the vessel after ligation of the common carotid artery. Unless the internal carotid is ligated above the bifurcation it is possible, through collateral circulation, for arterial blood to descend via the external carotid and thence up to the internal carotid, thereby offering a chance for further bleeding. Common carotid ligation is not only technically easy and quick but lessens the chances for subsequent

cerebral damage. However, if hemorrhage continues nothing remains but ligation of either the internal or the external carotid and the acceptance of the risk to the brain.

The accessory complications of cervical gland infection and mastoiditis served to prolong the clinical course and to retard the patient's convalescence, but these were essentially unrelated to the major pathology. In spite of repeated hemorrhage from the left ear no middle ear infection developed. The therapeutic value of blood transfusions in such instances of carotid hemorrhage is obvious. In the present case the patient received nine transfusions, but their effectiveness was only transitory until the gross hemorrhage was controlled.

319 LONGWOOD AVE.

## A LARYNGEAL PERPLEXITY

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To me the combination of diagnosis and management is always productive of food for thought. This is especially true where circumstances not infrequently spell failure. In such instances recoveries leave interpretation open to conjecture.—as is often the case in death without autopsy. Those acrimonious polemics which sometimes ensue in the wake of a dead patient seldom serve any purpose other than to confuse the issue and initiate the kind of feud that is well known in professional circles.

A classical example of a splendid contribution to medical literature can be said to be that of the late Dr. J. E. MacKenty. So instructive is his report that I have had the essential history and drawings from his original article framed for permanence. I use it to demonstrate to graduate students the difficulties encountered in the diagnosis of laryngeal disease.

The obtainment of an accurate history, direct and indirect laryngeal examination, thorough physical and neurological examination, supplemented by complete laboratory investigation (including roentgenography and microscopic study of secretions and tissue)

should make one reasonably certain of arriving at a diagnosis. Improper technic (or even the chance failure of not removing tissue sufficiently deep or from the affected site) and the possible, certainly not the improbable, presence of more than one finding to account for the laryngeal disturbance may completely throw the clinician off in the evaluation of a given case. Coexisting syphilis and tuberculosis or carcinoma lead to many controversial situations. Benign and malignant lesions are also capable of "stumping the experts." Even histologic technic and diagnostic interpretation often lack unanimity and uniformity. The management of laryngeal disease too often suffers from disagreement as to diagnosis; then too, controversies frequently arise as to whether medical treatment or surgical approach should be instituted.

One of my most interesting cases concerned a 69 year old railroad employee who has been observed at my clinic at the Research and Educational Hospital for the past seven years. I first saw him on October 23, 1933. He had begun to lose his voice five months before. Prior to this time three laryngeal biopsies, revealing no evidence of malignancy, had been taken at another institution. His tonsils and teeth had been extracted some six years before and he had had a sinus operation because of asthma.

Examination of his nose revealed some polypoid changes. The larynx showed swollen false cords, almost reaching the midline on phonation; the true cords were thickened and covered with a greenish crust. This process was bilateral. The motility of the cords was good. The physical examination revealed nothing abnormal; the X-ray of the chest and the blood serological findings were negative; and repeated sputum examinations made both by direct smear and from expectorated material were negative. Fungi were never found.

In the period of time from 1933 to 1939 eighteen biopsies were performed. The original biopsy revealed an intact overlying squamous epithelium with the underlying stroma displaying no abnormalities. Other biopsies showed a papilloma, and again a hyperkeratotic process. At these times there was a stratified squamous epithelium thickening characterized by hornification. The basement membrane was well preserved and there was no tendency for invasion. This biopsy followed laryngofissure, performed for the purpose of more accurately determining the exact pathology. It was not until August 11, 1936 that fragments of tumor tissue revealed a probable squamous cell carcinoma. Another biopsy taken ten days later displayed islets of anaplastic squamous cells, in papillary arrange-

ment, with some early pearl formation. It was then believed that we were dealing with a hornifying squamous cell carcinoma. But subsequent biopsies showed benign papilloma, as late as 1938, and it was felt that it was a possible malignant transformation of a benign papilloma. However, even this was not conclusive.

For purposes of diagnosis and therapeutics 37 direct laryngoscopies were performed, chiefly for biopsy and to relieve the airway, particularly when the larynx was obstructed by the recurrence of hard, white masses on both vocal cords. Electrocoagulation was undertaken on several occasions; dilatations of the stenotic larynx were performed twice in 1939, and of the esophagus 13 times in 1939 and 1940. On January 8, 1935 a laryngofissure, already alluded to, was done. Severe bleeding ensued after biopsy, and a low tracheotomy had to be done. A postoperative bronchopneumonia followed. Following irradiation on October 26, 1936 a gastrostomy was advised since the patient had been unable to take fluids for over a week. Gastrostomy closure occurred February 2, 1938, but after this he developed an incisional hernia. On May 14 of that year embarrassed respiration required an emergency tracheotomy; again a stormy course of bronchopneumonia ensued. He still carries this tracheotomy, and numerous tracheal difficulties due to crusts and fungating masses have made after-care one series of emergencies after another.

From November 1933 to December of that year the patient received 1200 roentgen units on each side of the neck. This was given at a time no proof of malignancy was evident. When the biopsy revealed carcinoma he received 2400 roentgen units. The irradiation, however, produced no effect upon the neoplasm, but the local reaction produced necessitated the gastrostomy that has been described. On several occasions, and particularly during the bronchopneumonia episodes, the patient showed signs of dementia. He often threatened his own family. At the present writing he is confined to a psychopathic hospital. The laryngeal lesions remains about the same — with whitish verruca-like masses in the larynx and a papillary excrescence surrounding the tracheotomic wound.

This laryngeal case, covering a period of seven years, presented so many diagnostic and therapeutic difficulties that it can readily fall into the category of an unusual case. Biopsy throughout the course was imperative, but apparently has not solved the major problem. Whether the lesion was benign to begin with, undergoing malignant degeneration following therapy, is a point in question. The bilateral

nature of the lesion together with failure to respond to the customary therapeutic measures adds to its complexity. The repeated tissue examinations, the findings of benign and later of malignant tissues, and then again the benign, have made interpretation difficult. It is quite possible that much could have been accomplished had a total extirpation of the larynx been done in the early years. In retrospect, however, what already has been done might again be repeated under similar circumstances.

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# The Scientific Papers of the American Broncho-Esophagological Association

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XCVII

## THE SURGICAL TREATMENT OF CARCINOMA OF THE THORACIC ESOPHAGUS: CASE REPORT WITH DESCRIPTION OF NEW ARTIFICIAL ESOPHAGUS\*

JULIAN JOHNSON, M.D.

PHILADELPHIA

For many years it has been the almost universal custom in the medical profession to look upon carcinoma of the esophagus as a completely hopeless condition. Once the diagnosis was made the internist lost all interest in the case. The surgeon might be prevailed upon to perform a gastrostomy for feeding purposes but immediately set the patient aside as a candidate for a nursing home for the rest of his life. The radiologist at best could offer only palliative therapy. In short, the medical profession to a great degree had adopted the attitude toward cancer of the thoracic esophagus which the general public held toward cancer in general.

This attitude of the medical profession was justified in part, for prior to 1934 there were only 14 successful resections of carcinoma of the thoracic esophagus, the first having been performed by Torek in 1913. Torek's patient lived 13 years and died of pneumonia without recurrence of the carcinoma. Thus, the surgical management of carcinoma of the esophagus had not kept pace with that of carcinoma elsewhere. This was largely due to (1) difficulties in surgical technic, (2) difficulties of making an early diagnosis.

It is my purpose to call attention to the fact that the difficulties in surgical technic have now been overcome to a great degree. I do not mean to imply that there are no longer any surgical problems

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\*From the Surgical Clinic of the Hospital of the University of Pennsylvania.

Presented at the 24th annual meeting of the American Broncho-Esophagological Association, Cleveland, Ohio, June 3, 1941.



to be solved, but I do want to point out that the surgical technic is now sufficiently standardized so that a reasonable surgical mortality may be expected if the operation is performed upon patients who are reasonably good surgical risks.

Perhaps it would be worth while to call attention to some of the factors which have increased the safety of these operative procedures.

The esophagologist has been of the greatest aid to the surgeon in the proper selection of the patients for operation. Without his aid an early diagnosis is almost impossible. The diagnosis may be suspected by the history and confirmed by X-ray examination, but one hesitates to subject a patient to the resection of the thoracic esophagus until a positive diagnosis is made by biopsy.

Perhaps the greatest advance in thoracic surgery has been in the field of anesthesia. In the old days, when a surgeon opened a chest, he immediately found himself in a race against the death of the patient from anoxia. It was a question of whether he could do his operation and close the chest before the patient died. Extra-pleural operations were attempted to avoid this difficulty but without great success. Today this difficulty has been overcome by intratracheal anesthesia so that the physician-anesthetist may keep the patient properly oxygenated at all times. The surgeon may now open the chest widely enough to adequately expose the operative field, and proceed with the operation in an unhurried manner, taking two or three hours if need be.

One of the greatest causes of death in these patients has been infection in the mediastinum. Because of the necessity of closing the chest in order to allow proper aeration of the lung, the operative site could not be adequately drained to guard against infection. Today, however, a large tube is placed into the chest as a drain in the event of infection. Negative pressure of 8 to 10 cm.  $H_2O$  is constantly applied to this tube so that the lung is kept expanded. If infection does occur it is readily drained.

Many little improvements in technic have helped decrease the possibility of contamination of the wound at the time of operation. Moreover sulfonamide therapy has been a great help in the prophylaxis against infection.

These improvements in teamwork and technic have undoubtedly helped greatly in the surgical treatment of carcinoma of the thoracic esophagus. Although only 14 cases were successfully operated upon up to 1934, Adams found reports in the literature of 49



Fig. 1. Artificial esophagus.

successful operations from 1934 to 1940. The longest survival of these patients had been four years. To this list of patients with carcinoma of the thoracic esophagus successfully operated upon we would like to add another.

#### REPORT OF A CASE

W. H., male, aged 57, first noticed difficulty in swallowing about the middle of October 1940. He went to his physician after about two weeks. His physician X-rayed him for swallowing function and noted a defect. He sent him to Dr. Gabriel Tucker who found a squamous cell carcinoma of the esophagus at about the mid-thoracic region. Dr. Tucker felt that this was an early lesion and might be suitable for resection. The patient had lost only about 10 pounds in weight and appeared to be in fairly good condition. A Janeway gastrostomy was done about the middle of November 1940. He regained his weight, and on December 11, 1940 a resection of the thoracic esophagus was done. This was done in a manner similar to that described by Torek originally. A posterior approach was used. The fifth rib was resected and the fourth and sixth ribs were cut. The lung was pushed forward and the esophagus was exposed. The tumor was located at about the level of the bifurcation of the trachea. It was freed from the trachea with some difficulty. There were no enlarged glands. The esophagus was cut off at the lower end and inverted into the stomach. The esophagus was then resected above the tumor and the upper end protected by a rubber tissue. The dissection was then carried up into the neck and the pleura closed with the esophagus above it. The chest wound was closed, and the esophagus was

then delivered through a cervical incision. The esophagus was brought out through an incision in the skin at the first interspace. A tube was placed in the chest for constant suction. The patient's convalescence was quite uneventful.

The esophageal fistula was connected with the gastrostomy by a rubber tube for feeding purposes. Some difficulty was encountered by leakage around the esophageal fistula because of the sudden increase in pressure in the tube during the act of swallowing. This was avoided by incorporating a rubber balloon in the rubber tube to take up the pressure. This rubber balloon is the bladder from a child's football sold at all sports goods stores for fifty cents. As shown in Fig. 1 the connections are made of metal. At the upper end a side arm allows swallowed air to escape and not be pushed down into the stomach. At the lower end is a clamp which may be closed when the patient is not eating so that he may bend over in his work as a mechanic without any spilling. While eating the patient may force the food down more rapidly if desired by a milking action on the rubber balloon. The apparatus is held in place by a leather strap around the neck. The gastrostomy tube is held in place by an elastic belt so that no adhesive is required on the skin. The small piece of adhesive on the air vent shown in the illustration has been dispensed with by connecting the rubber tube to the leather strap around the neck. With this apparatus the patient has been able to eat normal meals, providing his meat is ground. The time consumed in eating a meal is very little more than normal. It has now been six months since operation, and the patient has returned to work as a skilled mechanic.

This case report merely serves as an example of the fact that the difficulties in surgical technic in the surgical treatment of carcinoma of the esophagus have been overcome to a great degree. It is true that the mortality is still high when the operation is done as a last resort, after the carcinoma has already spread or the patient has lost a large percentage of his body weight. But if the patient is operated upon early when he is still a reasonable operative risk, a low mortality may be anticipated. The cooperation between the surgeon, the esophagologist and the physician-anesthetist has made this possible. This has been admirably demonstrated by Garloch and his associates, who have had seven operations with one death, a mortality of only 14%.

Nevertheless, in spite of the fact that the surgical difficulties have been overcome to a great degree, the fact remains that only about 70 patients have been successfully operated upon for a condition which constitutes about 8% of all malignant tumors in adults. It is obvious therefore that the problem here is the same as for cancer elsewhere, namely, early diagnosis.

There can be no doubt that carcinoma of the esophagus is frequently difficult or impossible to diagnose early. There are patients who have already passed the stage of operability before the first symptom occurs. There are others who put up with the dysphagia until they are inoperable before going to a physician. But there are

many who go to a physician with dysphagia and are treated conservatively until they become inoperable.

If further advances are to be made in the surgical treatment of carcinoma of the esophagus the public must be taught to regard dysphagia as seriously as a lump in the breast. The physician must be taught to investigate the slightest difficulty in swallowing and not wait until the diagnosis is obvious.

For many years the medical profession felt that there was no incentive to making an early diagnosis for carcinoma of the esophagus. The physician would reason that if there were no organic basis for the dysphagia it would disappear in a few days, while if it were carcinoma, nothing could be done anyway. So the policy of watchful waiting was frequently adopted.

I have no doubt, however, that as the medical profession becomes convinced that the successful resection of a carcinoma of the thoracic esophagus is the reward of early diagnosis and not a surgical curiosity, then and then only can we expect materially to increase the salvage rate in carcinoma of the esophagus.

#### SUMMARY

- 1.) A case report is given of a successful resection of the thoracic esophagus for carcinoma.
- 2.) A new type of artificial esophagus is described.
- 3.) It is pointed out that with the advances in thoracic surgery within recent years, the operations for carcinoma of the thoracic esophagus are sufficiently well standardized to insure a reasonably low operative mortality.
- 4.) It is suggested that early diagnosis offers the greatest opportunity for further improving the results of the treatment of carcinoma of the esophagus.

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## XCVIII

### FURTHER STUDIES ON THE TREATMENT OF ESOPHAGEAL VARICES BY INJECTION OF A SCLEROSING SOLUTION\*

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The treatment of esophageal varices by injection of a sclerosing solution into the veins through an esophagoscope has been a source of considerable interest to esophagologists. Last year, I<sup>1, 2</sup> reported my initial experience with this form of treatment. Since then, it has been my privilege to treat ten additional patients suffering from varices of the esophagus.

In order to better understand the rationale for treating varices of the esophagus by injection of a sclerosing solution, it is advisable to review briefly some of the mechanism involved in their production. The etiology underlying the development of esophageal varices is not known definitely. Two theories generally are advanced to account for their development: one school of thought has expressed the opinion that the primary difficulty is attributable to a disturbance of the vascular regulatory apparatus of the spleen, so that the arterial blood flows unobstructedly into the venous system and produces an effect analogous to that of an arteriovenous fistula. The other school of thought postulates that the difficulty arises as a result of obstruction in the splenic or portal vein owing to either intrinsic or extrinsic causes, producing obstruction to the free passage of blood back to the systemic circulation and giving rise to a state of portal or splenic hypertension. In either case, there occurs marked congestion of blood in the portal circulation owing to inability of the splenic or portal veins to return the blood adequately to the systemic circulation.

Nature attempts to compensate for the difficulty and to establish new channels to return the stagnant blood to the general circulation. This attempt as a rule takes place through channels of communication that already exist between the portal and the systemic

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\*Presented at the 24th annual meeting of the American Broncho-Esophagological Association, Cleveland, Ohio, June 3, 1941.

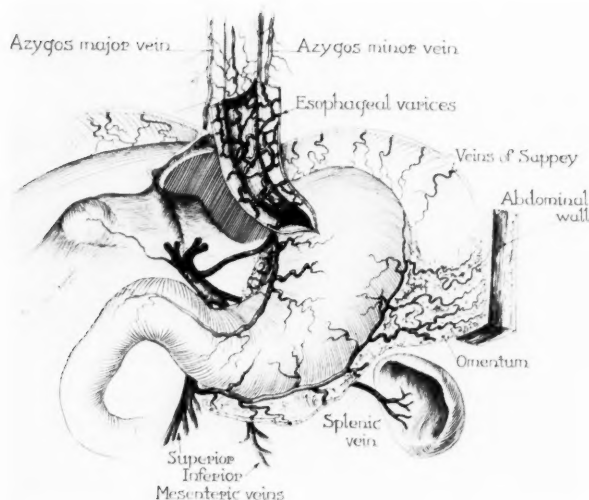


Fig. 1. Diagram illustrating purpose of injecting esophageal varices.

circulation. The anastomosis that most frequently results and with which we are most concerned is that which leads to the development of esophageal varices. This anastomosis, as McIndoe<sup>3</sup> pointed out, is by way of the coronary vein, which likewise is the most direct method of communication between the portal and the systemic circulation.

Kegaries<sup>4</sup> demonstrated the manner in which anastomosis takes place between the portal and the caval circulation by way of the cardia and the lower portion of the esophagus. The coronary vein of the stomach branches as it pierces the muscular coats to reach the submucosa of the cardia, where it divides into a number of small, longitudinal venules which have no cross communication for 3 or 4 cm. At this level, they break up into a rich plexus which anastomoses freely and which may extend into the upper third of the esophagus. Communicating branches run from the plexus to large periesophageal trunks which in turn communicate with the azygos, the intercostal and the diaphragmatic veins of the systemic circulation. The veins in the submucosa of the esophagus are very poorly supported by loose connective tissue. As a result, varices develop because of

the increased flow of blood through the veins and the inability of the muscular and elastic fibers to withstand the increased venous pressure. In addition, the tendency toward the formation of varicosities is accentuated by the effect of changing suction which takes place in the thoracic cage with respiration.

Theoretically, the purpose of injecting a sclerosing solution into esophageal varices is to block the free passage of blood through the esophageal veins (Fig. 1). By doing so, one hopes to stimulate the portal circulation to increase its efficiency in conveying blood back through the liver to the systemic circulation in a normal manner. Of probably even greater importance is the stimulation of new anastomotic channels to convey the blood from the portal to the systemic circulation by such a route that the communication will not be subjected to trauma as occurs in the esophagus.

The diagnosis of esophageal varices all too often is made only at the postmortem table. The condition should be suspected in any case in which there is a history of unexplained massive gastrointestinal bleeding. Careful roentgenographic examination of the esophagus usually will reveal the presence of varices. Occasionally, the diagnosis can be made only on esophagoscopy examination, as was true in one of the 11 cases (Table I, Case 6) which I am reporting herein. The roentgenographic appearance of esophageal varices is well illustrated in Figs. 2, 3 and 4.

Esophageal varices as seen through the esophagoscope present a characteristic picture (Fig. 5). The varices appear as tortuous, often nodular, light bluish prominences which protrude into the esophageal lumen. They are easily compressible and change in shape with peristalsis of the esophagus. They tend to run in a longitudinal plane, and may be so large and numerous that they occupy the entire esophageal lumen, producing dilatation of the esophagus.

Many procedures have been advocated for the prevention and control of bleeding from esophageal varices. Up to the present time, splenectomy is the procedure that has given the most satisfactory results in cases in which the esophageal varices were due to splenic anemia. W. J. Mayo<sup>5</sup> pointed out that this procedure should be of value if for no other reason than that removal of the spleen decreases by about 20% the amount of blood that passes through the portal circulation, thus lessening the amount of blood that must be transported back to the systemic circulation by the portal system. Kegaries emphasized that in splenectomy the vasa brevia that communicate with the esophageal veins are severed also, thus eliminating



Fig. 2. Punched-out defects in the roentgenographic shadow, characteristic of esophageal varices.



Fig. 3. Defects along edges of roentgenographic shadow of opaque mass, characteristic of esophageal varices.

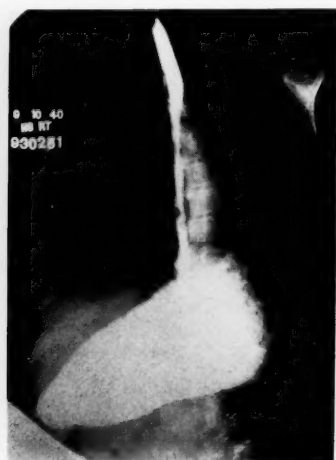


Fig. 4. Defects along edges of roentgenographic shadow of opaque mass, characteristic of esophageal varices.



TABLE I  
CASES IN WHICH SPLENECTOMY HAD BEEN PERFORMED  
PREVIOUS TO TREATMENT OF ESOPHAGEAL VARICES  
BY INJECTION

Case	Diagnosis	Age, Years, Sex	Frequency of Hemor- rhages, months	Duration of Trouble After Splen- ectomy, years	Injections of Solution		Hemor- rhages Subsequent to Treat- ment	Time Elapsed After Injection, months
					Num- ber	Amt., cc.		
1.	Banti's disease	30 M.	3	4	8	13	2	15
2.	Splenic anemia	20 M.	3	11	14	38	1	10
3.	Splenic anemia	11 F.	4	3	9	15.5	1	8
4.	Throm- bosis of splenic vein	33 M.	3 or 4	1	12	33	0	5
5.	Splenic anemia	18 F.	4	2	4	12	0	3
6.	Splenic anemia	16 F.	4	$\frac{1}{3}$	3	7	0	2

a possible source of communication between the portal and the caval circulation. Recurrence of hemorrhage subsequent to splenectomy is, however, not unusual. Pemberton<sup>6</sup> reported that recurrence of hemorrhage from esophageal varices after splenectomy takes place in approximately 50% of cases, and that bleeding from esophageal varices is a frequent cause of death. It becomes readily apparent, therefore, that any procedure that can prevent such bleeding is worthy of serious consideration. In 1933 Pemberton<sup>7</sup> and Walters<sup>8</sup> each suggested the advisability of injecting a sclerosing solution into esophageal varices, either through an esophagoscope or into the coronary vein at time of surgical intervention. With the aid of Dr. Bollman, I attempted to produce esophageal varices in experimental animals so that the effect of injection of a sclerosing solution into varices through an esophagoscope might be determined. Much to our chagrin, although we could produce enlarged vessels over the thoracic wall of an animal, we were unable to produce enlargement of the veins in the esophagus. Consequently, the idea of employing the method in treatment of the human being remained in abeyance.

It remained for Crafoord and Frenckner<sup>9</sup> of Stockholm to report, in 1939, the first successful injection of esophageal varices with a sclerosing solution through an esophagoscope. Their success encouraged me to attempt to duplicate their procedure. The equipment I employ in the injection of esophageal varices is based on Crafoord and Frenckner's original description.

In order to afford better illumination, I have devised an esophagoscope which has been found especially useful for this type of work (Fig. 6). The instrument possesses both distal and proximal illumination. The tip of the instrument is similar to that employed by Haslinger, and the proximal end of the esophagoscope has a flare to one side to permit use of the Negus electroscope. The apparatus

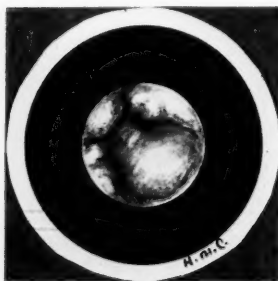


Fig. 5. Appearance of esophageal varices as seen through an esophagoscope.

for injection consists of a firm, 11-gauge tube to the end of which a 24-caliber hypodermic needle is attached. The proximal end of the tube is bent at a right angle to permit free visualization. To the proximal end of the tube a short piece of rubber tubing is fitted to allow for the attachment of the syringe containing the sclerosing solution. The use of a rubber connection is of great value in preventing unnecessary jiggling of the needle during the period of injection. A removable handle which can be attached to the proximal end of the needle has been found of considerable assistance in guiding the needle properly and steadily.

Crafoord and Frenckner employed a solution of quinine hydrochloride as the sclerosing agent. For this solution I have substituted a solution of sodium morrhuate because it is less likely to produce slough and severe systemic reaction. At first, a 2.5% solution of sodium morrhuate was employed, but at the present time a 5% solution is being used because it seems to produce somewhat better and more rapid sclerosis, with no increased discomfort or risk to the patient.

The injections are carried out with the patient under local anesthesia. The esophagoscope is passed to the desired level, and a suitable vein is selected for the injection. The injection is facilitated by making light pressure with the end of the esophagoscope against the vein just proximal to the point at which the needle is to be

inserted. The needle then is inserted into the vein. Should there be doubt that the needle is in the lumen of the vein, a small amount of blood can be aspirated back into the syringe to make certain of this point. With the needle in proper position, the solution of sodium morrhuate is injected slowly into the vein. The amount of solution that should be injected at one time depends on the patient's reaction. I have injected as much as 9 cc. at one treatment without ill effect. It is well to limit the amount injected at the first treatment, to be certain that the patient is not sensitive to sodium morrhuate. Seldom can more than two veins be injected at one sitting. When the needle is withdrawn from the vein, there invariably occurs at the site of the puncture wound a small amount of bleeding, which usually can be readily controlled by pressure with a small cotton tampon. In two cases at the clinic severe hemorrhage occurred immediately on withdrawal of the needle from the vein. In the first case it was necessary to pack the esophagus with a gauze pack to control the bleeding; in the second case the bleeding was controlled by the topical application of fer-de-lance snake venom.

Most injections can be carried out without pain to the patient. At times injection will be associated with severe pain which is situated substernally and extends through to the back. The pain generally comes on after 1 to 2 cc. of the solution of sodium morrhuate has been injected, and if it occurs the treatment must be stopped. Whether the pain is due to escape of the sclerosing solution into the perivascular tissues or to a spasm of the vessel it is difficult to say. In no case has there been evidence of slough subsequent to such a reaction. The pain usually disappears in from 12 to 24 hours. In only one case in my experience has pain occurred with each injection.

The change that occurs in the varices subsequent to injection differs in various blood vessels. Some veins become firm, smaller, and pale. Others do not undergo immediate change in size but become firm and discolored and appear as though thrombi were present. The veins about the cardia and anterior wall of the esophagus are the most difficult to treat by injection.

The injections are repeated until most of the vessels have been treated. Usually, after four to ten injections, there may be difficulty in determining which veins are undergoing sclerosis and which are still open. In such an instance the patient is permitted to return home with advice to return in three months for examination and, if indicated, further treatment. Invariably after that period of time it is discovered that small veins have enlarged and that some of the injected varices, apparently having undergone canalization, again are

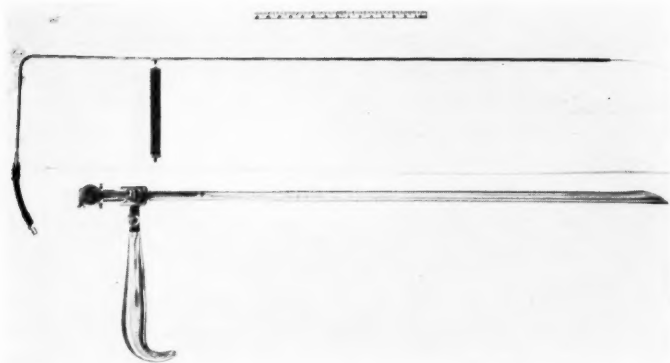


Fig. 6. Needle and esophagoscope used for injection of esophageal varices.

carrying blood. How often the procedure will have to be repeated is still unknown, nor is it known how effective the treatment eventually will prove to be.

The 11 cases in which I have treated patients for esophageal varices by injection of a sclerosing solution I have divided for purposes of study into three groups. The first group comprises those cases in which splenectomy was performed, with or without omentopexy or ligation of the coronary vein, before injection with a sclerosing solution was undertaken. The second group consists of cases of esophageal varices in which attempt at surgical relief had not been made. The third group comprises cases of esophageal varices in which treatment by injection of a sclerosing solution was given first and splenectomy was done subsequently. In each case, the major complaint was that of gastrointestinal hemorrhage.

The six cases in the first group are listed in Table I. In five of the six cases diagnosis was made of esophageal varices attributable to splenic anemia or Banti's disease. In the other case (Case 4), the esophageal varices were thought to be due secondarily to a portal thrombosis. The patients were divided equally as to sex. The youngest patient was 11 years of age and the oldest, 33. Five of the six patients had suffered from hemorrhage from the esophageal varices before splenectomy was performed. In one case (Case 5), the spleen had been removed because of splenic enlargement and general debility. In two cases (Cases 1 and 5) the patients had been

free from hemorrhage more than seven years subsequent to splenectomy before bleeding recurred. In all the others, recurrence of bleeding from the varices took place within less than a year after splenectomy.

When hemorrhage is mentioned in discussion of cases of this type, reference is not made to a slight loss of blood by stool. Hemorrhage invariably means that the patient vomits a large amount of blood or passes blood copiously by stool, or loses blood by both ways. The loss of blood amounts to one or two liters or even more with each hemorrhage. The concentration of hemoglobin invariably drops below 40%, and in one case in this series (Table II, Case 10), it dropped below 18%. Shock and coma are frequent with severe hemorrhage. Each of two patients (Table I, Case 1 and Table II, Case 9) estimated that within a period of six years he had lost considerably more than 50 gallons of blood from hemorrhage.

In the cases in the first group the period during which hemorrhage occurred, between the performance of surgical operation and the institution of treatment by injection, varied from four months to 11 years. The average length of time between hemorrhages in these cases was from three to four months.

The number of injections that were carried out in each case and the amount of solution of sodium morrhuate injected are stated. The greatest number of injections given in any case in this group was 14, and the largest total amount of solution injected was 38 cc.

Three of the patients, at the time this report is written, have had bleeding from the esophageal varices subsequent to treatment, but in only one case was the hemorrhage as severe as before treatment was instituted. In one of the cases in which there has been recurrence of bleeding, I am certain that sufficient of the sclerosing solution has not been injected. One patient (Table I, Case 2) has varices in the stomach as well as in the esophagus. It is doubtful that these gastric varices can be reached by the present form of treatment. It may be that to inject the sclerosing solution into the veins at the time of splenectomy, as was done by Grace, will prove to be a more satisfactory method of dealing with gastric varices.

Attempt was not made in any case to restrict the patient's diet after the injections or to keep the blood volume down. I am doubtful that the character of food ingested has a great deal to do with the production of bleeding from esophageal varices. It is more likely that acute infections and strenuous exertion are contributory factors.

TABLE II  
INJECTION TREATMENT FOR ESOPHAGEAL VARICES

Case	Diagnosis	Age, Years	Sex	Frequency of Hemorrhages, months	Duration of Trouble, years	Injections of Solution, Num-ber	Amt. cc.	Hemorrhages Subsequent to Treatment	Time Elapsed After Injection, months	Dye Retention, grade
CASES IN WHICH SPLENECTOMY HAD NOT BEEN PERFORMED PRIOR TO TREATMENT BY INJECTION										
7.	Cirrhosis of liver	56	M.	3	1½	6	15	0	6	1
8.	Cirrhosis of liver	40	M.	6	1	1	?	0	13	2
9.	Cirrhosis of liver (?)	36	M.	2	6	27	50	1	11	3
CASES IN WHICH SPLENECTOMY WAS PERFORMED AFTER TREATMENT BY INJECTION										
10.	Banti's disease	48	M.	1	2	14	21	0	4	
11.	Banti's disease	52	F.	1*	1/12	11	9.5	1	1½	

\*Only one hemorrhage had occurred prior to injection.

The second group, consisting of cases in which bleeding from esophageal varices had occurred but in which splenectomy had not been performed, is charted in Table II. The diagnosis in Cases 7, 8 and 9 in this group was of cirrhosis of the liver, although there is some question as to whether the pathologic condition in Case 9 was not really Banti's disease. These patients were all men and were older than the patients in the first group. The cases were characterized also by the fact that tests of hepatic function revealed that damage to the liver had taken place, as signified by retention of dye. The third patient (Case 9) included in this group received the greatest number of injections and largest total amount of solution administered to any one patient in the series.

Cases 10 and 11, in the third group, which is included in Table II, are of especial interest for they afforded an opportunity to determine whether, after a sclerosing solution has been injected into esophageal varices, nature attempts to establish new anastomotic communications between the portal and the systemic circulation. In each case a clinical diagnosis of Banti's disease was made. It was only after injections had been given that enlargement of the spleen developed and the causation of the esophageal varices was established definitely. In the first case (Case 10) in this group, the patient had two hemorrhages during the time the injections were being given but did not experience bleeding subsequently. In the other case (Case 11), bleeding occurred within two weeks after the last injection. Because of the rapid enlargement of the spleen, splenectomy seemed advisable in each case. At operation, the surgeon discovered evidence that the cardial end of the stomach and the under surface of the diaphragm were the site of much more intense inflammation than normally is encountered in cases of splenic anemia. He found, furthermore, that larger blood vessels than usually are present were evident over the under surface of the diaphragm, a phenomenon which seemed to indicate an attempt on the part of nature to establish an anastomosis.

Sufficient time has not elapsed to determine with accuracy the efficacy of the injection type of treatment of esophageal varices. Time undoubtedly will bring about modifications of the present technic and may even prove the procedure to be useless. For the present, our experience has been encouraging and the patients, for an unknown reason, state that their general health has been improved since the treatment was instituted.

MAYO CLINIC.

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XCIX

ESOPHAGEAL NEUROSES\*

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The purpose of this paper is to call to your attention a small number of patients exhibiting a complaint of definite type though not of specially serious nature. Their complaint is that they can not swallow certain articles of food or certain forms of medication, yet they have no difficulty in deglutition of other substances which require the same or greater effort to carry them past the natural points of physiological pause in the act of swallowing. Fanciful or hysterical, the physician may say, yet to the patients the trouble is a definite thing and often a positive embarrassment, and they come to us as laryngologists for help. You have all no doubt observed such patients, but the natural tendency may often have been to dismiss them as purely neurotic and to make no special attempt to alleviate the symptoms.

This discussion is to be brief, and it is presented principally because, so far as can be determined, patients of this type have not heretofore been described as a class. The subject is not thought to be of grave importance in itself, but from the scientific standpoint certain interest attaches to it.

It is to be understood that as a rule these patients do not give a history of trauma of the larynx or esophagus, either surgical, foreign body, or caustic erosion, with or without stricture. There is no spasm of either the upper or lower ends of the esophagus. There is no obstruction by either the aortic or bronchial narrowing. Some patients have been nervous and neurotic and others have definitely not exhibited these characteristics. Two types have been observed, patients who have difficulty with food, and patients who have difficulty with medication.

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\*Presented at the 24th annual meeting of the American Broncho-Esophagological Association, Cleveland, Ohio, June 3, 1941.

The patient having difficulty with food may state that certain forms of the article of food can not be swallowed, while other parts or differently cooked ones of the same food can be easily swallowed. In such an instance it would seem probable that the patient is a definitely neurotic individual. These neuroses are not permanent, and if the mental disturbance or worry can be determined and measures established to correct the mental attitude, together with procedures to convince the patient that there is no definite obstruction in the esophagus, the results are good.

The careful passage of a large (9 or 10 mm. x 45 or 53 cm.) esophagoscope with little or no anesthesia, the patient in either the recumbent or sitting position, is, we feel, a necessary procedure, and after a few treatments the patient is convinced that there is no organic obstruction. We regard this treatment as of equal importance with the restoration of the psychic balance.

Patients having difficulty with medication will state that they can not swallow a tablet or capsule, or, in some cases, certain liquid medication, and some of them refuse even to try. These patients can be divided into two classes, those who object to the taste or odor of a certain formula or medicament, and those who state that they can not swallow a tablet or capsule.

Those of the first class exhibit a neurosis or a purely hysterical manifestation, or just plain lack of effort or coöperation. They are like the patients who seat themselves in the examining chair and promptly state, "I can not tolerate anything on my tongue because I gag so easily." The extent to which patients of this class can be helped depends largely on their mentality and force of character. Morons (in either the lower or higher classes of society) we can hardly expect to educate to overcome this notion. Many of the more intelligent patients, however, can be cured of this idea by patient instruction and careful instrumentation.

The patient who states that a tablet or capsule can not be swallowed is often of a different type. Many of this class we would not, from their general demeanor or history, class as neurotic. Usually their difficulty is in faulty management of the tongue and oral muscles in the beginning of the act of deglutition. As we all know, once the tablet or capsule passes to the hypopharynx the difficulty is over. Patient instruction in the proper use of the tongue and management of the other oral muscles in the first acts of swallowing will correct this.

In the short time allotted it seems desirable to call your attention to the neural patterns or nervous pathways which use the muscle of the esophagus as their working tool or effector. These patterns may be arranged in a hierarchy with the least highly integrated or most automatic at the bottom of the scale and with the most highly integrated or least automatic at the top.

All of these patterns except the latter group, that is, the most highly integrated ones, are called partial or reflex patterns. These partial patterns do not use the mind or psyche, the highest level of integration in the nervous system, and the esophageal contractions which occur are usually some variation of the normal peristaltic movements. On the other hand, the most highly integrated or least automatic group, which are called total patterns, involve all of the levels of integration in the nervous system including the psychic. In these total responses the muscle of the esophagus acts as a tool of reaction patterns which express the drives and needs of the entire personality. As an organ, the esophagus is primarily concerned in getting nourishment from the environment. In this capacity it takes in some material and serves in the rejection of other matter.

Partial patterns are active in 1) the delivery to the stomach of food and water placed in the lower portion of the pharynx; 2) spasm of the esophagus due to irritation in the walls of the pharynx and esophagus; and 3) reflex contractions of the esophagus at the time of irritation in neighboring tissues which are supplied by the same segmental nervous mechanisms of the spinal cord as is the esophagus. This latter pattern is the one used in the so-called reflex contraction or spasm of the esophagus.

There are two degrees of severity in the derangement of the total patterns. The first type of case is the one in which the esophageal patterns are neurotic in type, but this does not mean that the entire personality can be called neurotic. The neurotic individual is essentially egocentric and is continually wanting and getting from the environment in order to satisfy his ego. In doing so he is constantly under tension, and his hyperactive esophagus may be a part of this tension. There may be a subtype who is rejecting something in the environment which threatens his ego. This is seen in the fear reaction. Either of these kinds of patients may show great variations in their esophageal tension from day to day. The treatment of this type of case is not easy and should be based on an understanding of the conflicts of the neurotic personality. Anything that will add to ego-security will lessen esophageal tension as was recently demonstrated by Faulkner.<sup>1</sup>

A second and less serious type of case is that of the individual who has been poorly trained and conditioned in the act of swallowing, either in general or for specific substances. This class also includes those who have been conditioned to gag or vomit easily. This type of patient should be treated by an intelligent or logical approach. He should be shown by the passage of the esophagoscope that his esophagus is intact and clear. Then he should be forced, in so far as possible, to do the thing which he has said he cannot do. If he is intelligent at all and if he is not essentially neurotic this procedure of demonstrating that it can be done should cure him.

These neuroses are usually not permanent. They can best be treated by a combination of psychotherapy and of common sense training in the effective use of the deglutition apparatus.

150 E. BROAD ST.

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CARCINOMA OF THE ESOPHAGUS WITH SPECIAL  
REFERENCE TO TREATMENT BY RADICAL  
SURGERY, X-RAY AND BOUGINAGE\*

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Carcinoma of the esophagus has long been regarded as a hopeless disease in which cure was impossible and palliative treatment unsatisfactory. I wish to call attention to the fact that with early diagnosis radical surgery may lead to cure and that even with late diagnosis X-ray treatment combined, if necessary, with bouginage may result in satisfactory palliation. It seems hardly necessary to point out that all patients complaining of difficulty in swallowing should have immediate X-ray examination. This should be followed by esophagoscopy in all cases of suspected neoplasm. Occasional cases of carcinoma of the esophagus are missed by X-ray examination and diagnosed by esophagoscopy. Since the reverse is also true, both methods must be used freely, and promptly repeated in doubtful cases. Sometimes two or even three esophagoscopies are needed in difficult cases before a positive biopsy can be obtained. If, under such circumstances, a second or third esophagoscopy is delayed more than a few days, the patient's chances of cure by radical surgery may be very much diminished. As in malignant disease anywhere in the body, all hope of cure depends upon early diagnosis.

Since Torek's first report<sup>1</sup> in 1913 of a successful esophagectomy for carcinoma, there have been reported in the literature 86 cases surviving esophageal resection with one three-year cure,<sup>2</sup> one four-year cure<sup>3</sup> and 10 five-year cures.<sup>4, 5, 6, 7, 8</sup> During the last three years, Churchill and Sweet have successfully resected five cases of carcinoma involving the middle esophagus and five cases of carcinoma involving the lower esophagus and the upper stomach. The most difficult region for successful resection is the cervical esophagus, and although Churchill<sup>9</sup> resected two in this location in 1933, both

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\*From the Massachusetts General Hospital.

Presented at the 24th annual meeting of the American-Broncho-Esophagological Association, Cleveland, Ohio, June 3, 1941.

recurred and the patients died within a year. Other cases have been explored and either found to be inoperable or the resection has been unsuccessful.

As an example of successful resection of carcinoma of the middle third of the esophagus I will cite the following case:

#### REPORT OF CASES

E. P., No. U-162314, a 43 year old housewife first came to my office October 26, 1938 complaining of pain after swallowing. Ten years ago the patient began having attacks of pain between the scapulæ on swallowing solid food. These attacks occurred on an average of three or four times a year for four years. Five years ago the symptoms became worse and she experienced difficulty in swallowing solid food and the pain was increased. X-ray of the esophagus at that time was negative. Ten months ago she experienced severe stabbing pain alternating between the interscapular region in the back and down the esophagus, occurring every fifteen minutes, lasting all night and severe enough to make her cry out. The pain was brought on by swallowing saliva or belching. Since then the swallowing had become increasingly difficult and for the past five months the patient had been unable to take solids, not so much because of the pain but because of apparent obstruction. Lately there had been regurgitation and vomiting even with liquids. There had been no nausea or hematemesis.

X-ray examination (Fig. 2) showed an obstructing lesion starting opposite the seventh dorsal vertebra and extending downwards for a distance of 4 cm. Within the area of obstruction there was an area of irregular but constant pattern suggesting ulceration. The findings were described as those of an ulcerating, constricting tumor of the esophagus, in all probability carcinoma.

The first esophagoscopy (EBB) was done November 10, 1938, and at a point 30 cm. from the upper incisors a firm, red, slightly nodular mass was encountered completely obstructing the further passage of the esophagoscope. Several biopsies were taken and bougies were passed. The biopsies were reported negative for carcinoma.

On December 8, 1938 esophagoscopy (EBB) was repeated and the same mass was encountered. Several biopsies were again taken but the pathological report showed only leucoplakia. Since we still felt that we were dealing with carcinoma esophagoscopy (EBB) was

repeated on December 22, 1938 and more biopsies taken, several of them from very deep within the narrow lumen. On this occasion the pathological report was epidermoid carcinoma, Grade III.

Since there was no evidence of metastatic disease and the patient appeared to be in good condition, she was prepared for operation by preliminary jejunostomy and several transfusions. On February 3, 1939 esophagectomy was performed by Dr. E. D. Churchill. The esophagus was first isolated on the left side of the neck. With the growth it was then dissected free through a right thoracic approach and the lower end was turned in. The upper end was then pulled out through the neck and the tumor cut off leaving an esophageal fistula in the neck. The final pathological report showed epidermoid carcinoma, Grade II.

Following a somewhat stormy convalescence owing to collapse of the right lower lobe and abscess in the upper end of the wound, the patient was ready on March 20, 1939 for second stage resection at which the distal esophageal stump was dissected from the posterior mediastinum and brought out on the skin. From then on multiple stage plastic operations were performed at varying intervals for the construction of a skin tube esophagus (Fig. 1). This anterior thoracic esophagus was completed in May 1940 and the patient is now in very good health, swallowing soft solids satisfactorily through the artificial esophagus. The X-ray appearance of this skin tube is shown in Fig. 3.

*Comment.* Several points in this case are worthy of comment. The long period of prodromal symptoms with one negative X-ray examination five years before admission might have led to a diagnosis of hysterical dysphagia. In fact the student who took the history commented that the patient was very neurotic and said he felt that practically all her symptoms could be due to hysteria.

The negative biopsy after the first two esophagoscopies might have led one to believe that carcinoma was not present and that we were dealing with a benign stricture. Under such circumstances one must pass the biopsy forceps well down into the lumen of the stricture to secure adequate tissue for a positive diagnosis of cancer. Since I have seen other cases of carcinoma of the esophagus treated for long periods of time under the mistaken diagnosis of benign stricture due entirely to false negative biopsy, I wish particularly to emphasize the fact that repeated esophagoscopies may be necessary. It is also to be noted that the biopsy report showed a Grade III lesion whereas the final report after esophagectomy showed only a

Grade II. The possibility of cure by radical resection should, therefore, not be denied to the patient on the basis of a high degree of malignancy, for as in this case, further study of the tumor may show the lesion to be of lower malignancy than was originally supposed.

This case, therefore, represents a two-year cure of carcinoma of the esophagus in a patient who had a long history and who apparently had a highly malignant growth from the first positive biopsy report.

A summary of the five cases in this group is shown in Table I.

Transthoracic esophagogastrctomy for carcinoma of the lower esophagus and upper stomach has aroused a great deal of interest recently. In an admirable review of esophageal surgery Bird<sup>10</sup> sums up the historical aspects of this operation as follows: "In spite of the fact that Biondi (1895), Sauerbruch in his early work, and Janeway and Green (1910) had worked out an apparently satisfactory endothoracic esophageal-gastric anastomosis on dogs and cadavers, no successes in human cases were recorded until Ohsawa's in 1933. Undoubtedly the greatest single advance in making this operation possible is the use of positive pressure intratracheal anesthesia. The first transthoracic esophagogastrctomy performed in this hospital was done by Dr. Churchill in 1939. The case report follows:

H. P. E., No. U-212595, a 59 year old salesman, was first admitted to the hospital September 18, 1939 complaining of hematemesis. During the past nine months he had lost his job, seen his capital disappear and had no prospect of work. Nausea, vomiting and anorexia climaxed one questionable episode of hematemesis. Since then he had felt better and eaten with good appetite without vomiting for the past 10 days. X-ray examination in another hospital had been suggestive of esophageal varices or esophageal polyp. The impression obtained from the history was that of a functional disorder.

X-ray examination (Fig. 4), however, showed a definite lobulated, stenosing tumor of the lower portion of the esophagus and the cardiac end of the stomach.

Ten days after admission esophagoscopy (EBB) was performed. The esophagoscope passed readily through a normal esophagus to a point approximately 35 cm. from the upper gum where a soft polypoid mass was seen arising from the right anterior wall of the esophagus. Two large satisfactory biopsies were taken from this



TABLE I

CASE	UNIT NO.	AGE	SEX	DURATION OF SYMPTOMS	PATHOLOGICAL REPORT BIOPSY	FINAL	SURGEON	DATE OF RESECTION	FOLLOW-UP
E.P.	162314	43	F.	10 mos.	Ep. Ca. III	Ep. Ca. II	E. D. Churchill	2-3-39	Living and well
R.B.	234193	48	M.	4-5 mos.	Ep. Ca.	Ep. Ca. III	E. D. Churchill	3-27-40	Living with recurrence
C.W.	220333	52	M.	5 wks.	Ep. Ca. II	Ep. Ca. II	R. H. Sweet	8-3-40	Living and well
A.M.	279893	59	M.	Few mos.	Ep. Ca. II	Ep. Ca. II	R. H. Sweet	1-9-41	Living and well
J.L.	401504	48	M.	4 mos.	Ep. Ca. I	Ep. Ca. I	R. H. Sweet	11-14-40	Living and well



Fig. 1. Case E. P., No. U-162314. Appearance of chest wall following completion of artificial skin tube esophagus. Note swelling in region of upper sternum.

lesion which appeared like a soft, cauliflower carcinoma. There was very little bleeding. A No. 24 esophageal bougie passed readily into the stomach. The biopsy was reported adenocarcinoma, Grade II.

On a dietary regimen the patient gained 25 pounds in weight. He was readmitted for operation on November 7, 1939. Transfusion was performed, and 10 days later Dr. Churchill resected the lower esophagus and the upper stomach by the transthoracic route. Under intratracheal positive pressure anesthesia the left chest was opened through the bed of the ninth rib. The left lower lobe was retracted upward. The diaphragm was cut transversely over the dome toward the esophageal hiatus. The upper abdomen was then explored and no evidence of metastatic disease found in the gastrohepatic ligament, right or left lobes of the liver, or in the retroperitoneal tissues. The esophagus was mobilized from the mediastinum for a distance of about four inches from the cardia. The fundus of the stomach was also mobilized after ligating the *vasa brevia* in the gastroligament and the vessels in the gastrohepatic omentum including the left gastric artery, thus making it possible to deliver the fundus and body of the stomach into the thorax. After resection of the growth an anastomosis was made between the lower end of the esophagus and the resected end of the

body of the stomach and omentum was wrapped around the anastomosis.

Convalescence was uneventful except for moderate pneumothorax which was treated by aspiration. A postoperative X-ray (Fig. 5) showed the anastomosis to be functioning well. Pathological report showed a polypoid, fungating ulcerating mass involving the lower esophagus and upper stomach. Microscopically the tumor was well differentiated. The periesophageal lymph nodes were negative.

Three weeks after operation the patient was discharged entirely relieved. He was followed in the Tumor Clinic and when last seen, September 18, 1940, was looking and feeling very well, eating everything. He weighed 170 pounds, a gain of 20 pounds since discharge.

*Comment.* It is a curious coincidence that in this case as in the preceding one the first impression was that of a gastric neurosis. A carefully repeated X-ray examination and esophagoscopy established the diagnosis and the nature of the tumor.

In view of a recent statement in the literature that carcinoma at the cardiac orifice of the stomach is inoperable, a few brilliant surgical results of this sort should be of interest to physicians as a whole and particularly to laryngologists and esophagoscopists who are likely to see such patients in their offices or on their first visit to the hospital.

Among other patients in this group there are several points worthy of comment.

A. D., No. U-94953, was a very frail-appearing woman of 68 on whom I performed an esophagoscopy January 31, 1931 and found epidermoid carcinoma, Grade III, of the lower end of the esophagus. X-ray appearance of this lesion is shown in Fig. 4. In a frail woman of this age with high grade malignancy and little esophageal obstruction I felt that all we had to offer her was X-ray treatment combined, if necessary, with bouginage. There was, however, no evidence of metastatic disease and Dr. Churchill successfully performed a resection of the lower end of the esophagus making a direct anastomosis with the upper end of the stomach (Fig. 5). Convalescence was uneventful and the patient was discharged entirely relieved 20 days following operation. The final pathological report showed the growth to be of Grade II malignancy. So here again as in the first case the biopsy specimen was misleading as to the degree of malignancy.

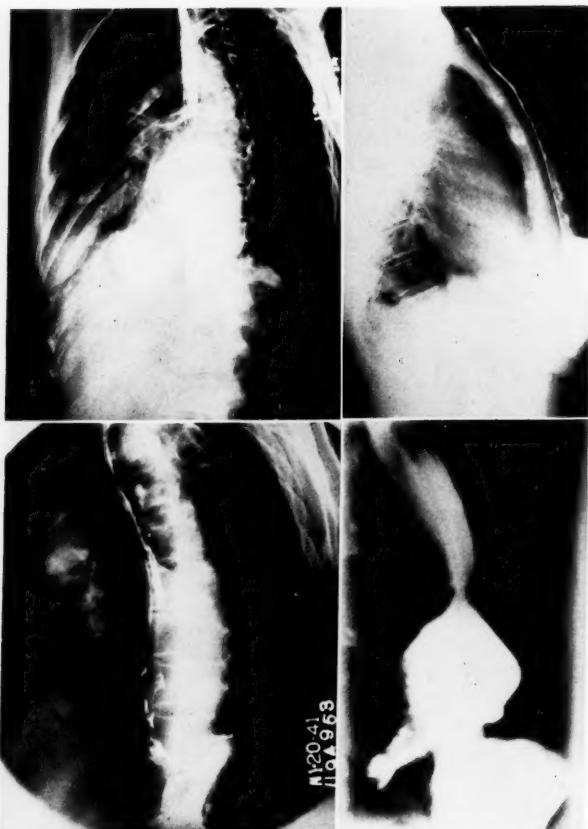


Fig. 2. Case E. P., No. U-162314. X-ray appearance of carcinoma of thoracic esophagus later successfully resected. Patient well two and a half years after resection.

Fig. 3. Case E. P., No. U-162314. Lateral X-ray showing barium in skin tube esophagus. Slight delay at lower end is aided by patient "milking" the food into the stomach.

Fig. 4. Case A. D., No. U-94953. X-ray appearance in this patient essentially the same as in case H. P. E. Lobulated, partially stenosing tumor of lower esophagus and cardiac end of the stomach.

Fig. 5. Case A. D., No. U-94953. Same general appearance as in case H. P. E. following resection of the growth showing stomach brought up into the thorax and anastomosed directly to the esophagus.

M. E. O'B., No. U-294086, was a 55 year old housewife who showed on X-ray examination a carcinoma of the upper end of the stomach and the lower end of the esophagus. On esophagoscopy (EBB), however, the lower end of the esophagus showed only an appearance consistent with leucoplakia, and biopsy obtained from this region showed no diagnostic abnormality. Nevertheless, at operation carcinoma was found involving the lower end of the esophagus and about two-thirds of the stomach. The esophageal nodules were small, firm and entirely submucosal, hence they were not visible by esophagoscopy. This case is, therefore, important in showing that under such circumstances esophagoscopy has its limitations.

A summary of the five cases in this group is shown in Table II.

Two other patients in this group also gave negative findings on esophagoscopy, and postoperative examination of the specimen in each case showed submucosal infiltration of the growth in the lower esophagus. It would, therefore, appear that a common form of extension for cancer of the upper end of the stomach is into the submucosa of the esophagus where it is impossible to see it by esophagoscopy. Reliance must, therefore, be placed on X-ray examination.

Palliative treatment for carcinoma of the esophagus includes radium and X-ray therapy, gastrostomy and bouginage. Present-day high voltage X-radiation is easier to administer and gives more satisfactory results than radium. Therefore, radium is no longer used in this hospital for the treatment of carcinoma of the esophagus. Since the more frequent use of bouginage combined with X-ray treatment, gastrostomy has rarely been necessary. Therefore, this discussion will be primarily concerned with the results of bouginage and X-ray treatment.

In a series of 55 consecutive cases of carcinoma of the esophagus in which I have performed esophagoscopy and which I have followed during the last three years the results have been as follows:

Ten patients have been operated upon as shown in Tables I and II. Three have been explored and found to be inoperable. One died a few weeks after resection. Seven have had gastrostomies, many of which could have been avoided by bouginage and X-ray treatment. Eight patients were not treated for various reasons, i. e., treatment was refused, or the patient was seen in a very late stage of the disease. The remaining 26 patients were treated either by X-ray or bouginage or both. Of these, 12 showed no sign of serious esophageal obstruction at any time and were treated by X-ray alone. Three were treated by bouginage alone but should probably

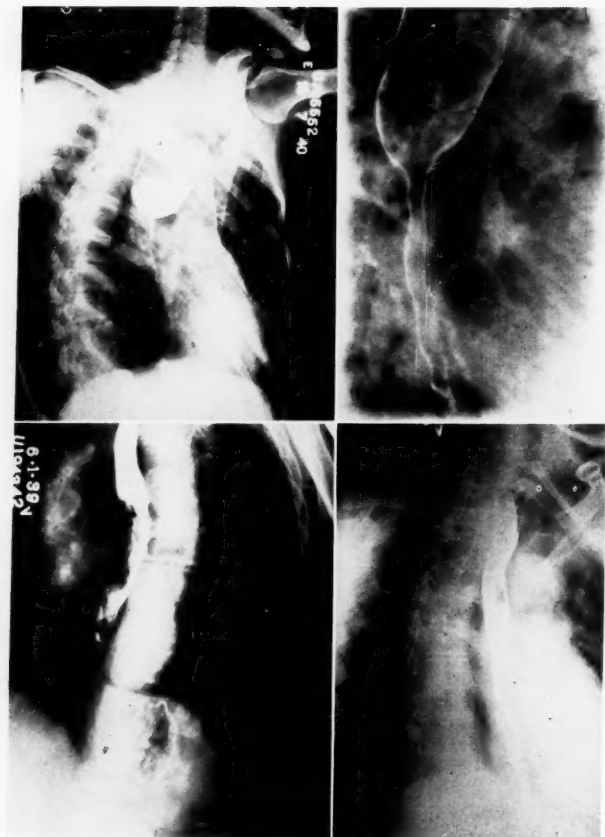


Fig. 6. Case H. C. D., No. U-195552. X-ray appearance showing carcinoma of the midesophagus reported by earlier X-rays and esophagoscopies to be a benign stricture.

Fig. 7. Case H. C. D., No. U-195552. Showing excellent lumen obtained following X-ray treatment and bouginage.

Fig. 8. Case C. G., No. U-194342. X-ray appearance of carcinoma before X-ray treatment.

Fig. 9. Case C. G., No. U-194342. Showing definite decrease in size of lesion following X-ray treatment.

TABLE II

CASE	UNIT NO.	AGE	SEX	DURATION OF SYMPTOMS	PATHOLOGICAL REPORT		SURGEON	DATE OF RESECTION	FOLLOW-UP
					BIOPSY	FINAL			
H.P.E.	212595	59	M.	3 mos.	Adenoca. II	Adenoca.	E. D. Churchill	11-17-39	Living and well
A.D.	94953	64	F.	3 mos.	Ep. Ca. III	Ep. Ca. II	E. D. Churchill	2-18-41	Living and well
M.E.O'B	294086	55	F.	1 year	Negative	Carcinoma	E. D. Churchill	4-2-41	Died postop.
P.B.	273238	68	M.	Few mos.	Negative	Adenoca.	E. D. Churchill	11-29-40	Living and well
W.F.	226834	48	M.	6 mos.	Negative	Signet ring cell carcinoma	R. H. Sweet	5-13-41	Living and well

have also received X-ray treatment. X-ray was withheld in these cases for two reasons: (1) the type of tumor, such as adenocarcinoma, was thought likely to show poor response to X-ray; (2) there was fear of perforation by bouginage of radiated tissues. In 11 patients bouginage, using a previously swallowed thread as a guide, was carried out in addition to the X-ray therapy. There have been no perforations. Although it is recognized that a perforation may occur, it is felt that the palliation obtained justifies the chance taken, for it is certainly true that patients very much prefer to eat by mouth than to be fed by gastrostomy. Some of these patients have been reduced to a diet consisting largely of liquids, strained vegetables and ground meat but others have been able to swallow normally and eat practically everything.

In the following case bouginage was carried out through the esophagoscope during a period of intensive X-ray therapy, following which the patient ate normally and returned to work.

H. C. D., No. U-195552, a 41 year old male, first entered the Baker Memorial Hospital, October 4, 1940, complaining of dysphagia.

Sixteen months prior to admission he had been treated for a year at another hospital where X-ray examination and two esophagoscopies were interpreted as showing a benign stricture. Bouginage was carried out with some relief, but no biopsy was taken.

On admission to the Baker Memorial Hospital the history given was that of increasing dysphagia with foul, blood-streaked sputum and recent hoarseness. There had been a recent loss of 18 pounds. The history dated back a period of 26 years when at the age of 15 the patient had some difficulty in swallowing described as spasm with spitting up of saliva and food. This continued intermittently for about three years, and then there were no further symptoms until two years prior to the present hospital admission. The recent episode consisted chiefly of dysphagia, cough, hemoptysis, loss of weight and hoarseness. A history of nervousness and irritability was obtained which led to a psychiatric consultation. Fortunately the psychiatrist although he considered the patient to be a compulsive neurotic and felt that psychiatric factors played a contributory role, recognized the fact that psychiatric approach would be a failure unless the organic side of the picture was carefully evaluated. X-ray examination was, therefore, repeated disclosing a carcinoma of the midesophagus (Fig. 6). Esophagoscopy was then performed (EBB) and showed a slit-like opening which bled easily and had a slightly



nodular margin from which a biopsy was obtained. The tissue from this area, however, did not look malignant. Bougies, sizes 10 to 24, were passed all the way through the narrowed area, and further biopsies taken from deep in the stricture which looked typical of malignant disease. The pathological report was carcinoma. Because of the patient's comparative youth, operation was considered, but bronchoscopy showed the left main bronchus to be narrowed and angulated as if from extrinsic pressure. There was a questionable metastatic shadow in the chest, and these findings together with the patient's hoarseness and long history made us feel that cure was out of the question. X-ray treatment was, therefore, given and esophagoscopy done once more for the purpose of bouginage during the course of the treatment. At the time of discharge he was feeling very much better and was able to eat a baked bean supper. The X-ray appearance of the esophagus following X-ray treatment is shown in Fig. 7.

Six weeks after admission the patient was discharged and was able to return to part-time work. Two weeks later he was eating normally. There had been a slight gain in strength. Ability to swallow normally continued up to the time of his death, the first week in February, 1941.

*Comment.* Here again we have a patient with a very long history of difficulty in swallowing treated for some time as a benign stricture, in whom the possibility of a neurosis was seriously considered. The diagnosis of carcinoma was made too late for successful resection, but a very good palliative result was obtained by X-ray treatment during the course of which the lumen of the esophagus was kept open by esophagoscopy and bouginage.

Although bouginage at the time of esophagoscopy is very useful, if the lumen is very narrow and bouginage has to be done frequently it may be more satisfactorily carried out by means of bougies passed over a previously swallowed thread as a guide. The patients may then be treated in the office or in the out-patient department. This program was carried out in the following case.

C. G., No. U-194342, a 64 year old housewife, first came to the hospital on May 23, 1939, complaining of vomiting of two months' duration. At this time she noted that food seemed to stick in the esophagus on swallowing. Sometimes a drink of water would enable her to swallow solid food more satisfactorily. There was, however, some vomiting of food and mucus but no hematemesis. Her appetite had been poor and she had lost 22 pounds in the past two months.

Physical examination was essentially negative. X-ray examination of the esophagus (Fig. 8) showed a sharp narrowing at a point just below the bifurcation of the bronchi with irregularity extending for a distance of 8 to 10 cm. The appearance was that of an annular carcinoma. Esophagoscopy (EBB) showed a large, red, fungating, nodular lesion having the typical appearance of carcinoma. Biopsies were taken, which were reported epidermoid carcinoma, Grade III. In view of the patient's age and general condition with a highly malignant growth, it was felt that radical surgery was out of the question. Accordingly X-ray treatment was instituted and was well tolerated. There was constant improvement in her ability to swallow for a period of about five months at which time X-ray examination (Fig. 9) showed a definite decrease in the size of the esophageal lesion although a definite defect was still present. At this time, however, the patient began to have some regurgitation, was feeling weak and had no appetite. She was able to get along satisfactorily straining all food eaten. Three months later she was having still further difficulty in swallowing, being unable to take any meat whatever even if finely ground up but taking some strained vegetables and liquids with regurgitation. Accordingly she was advised to swallow a thread and bouginage was instituted. After one passage of the bougie she was able to take mashed potatoes, crackers, strained vegetables and some ground meat. Bouginage was carried out every one or two weeks for a period of six months during which time she was able to eat soft eggs and mashed potato with, however, some regurgitation. Her ability to swallow in this manner continued up to the time of her death, October 4, 1940.

*Comment.* By X-ray treatment and bouginage a fairly satisfactory lumen was maintained in this patient until the time of her death. She was thus enabled to eat by mouth and a gastrostomy was avoided. It is felt that continued feeding by mouth is more satisfactory to these patients than palliative gastrostomy.

#### CONCLUSIONS

All patients with dysphagia must have immediate X-ray examination and esophagoscopy.

By early diagnosis an increasingly large proportion of patients with carcinoma of the esophagus may be cured by radical surgery.

The transthoracic approach has proved very valuable in surgery of the lower esophagus and upper stomach.

When patients are seen late in the disease, much can be accomplished in the way of palliation by X-ray treatment combined, if necessary, with bouginage.

Gastrostomy is seldom necessary.

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SO-CALLED ADENOMA OF THE BRONCHUS\*

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AND

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PHILADELPHIA

Among the benign tumors encountered in the bronchi the most important and interesting of all is that which is now most generally called bronchial adenoma. This type of tumor has also been called a carcinoid, a benign glandular tumor (Clerf and Crawford,) simply a tumor (Stout) and most recently a mixed tumor (Womack and Grahant). The pathologists encounter great difficulty in recognizing these lesions, and not infrequently call them carcinomas. On the other hand, they occasionally err in the other direction, mistaking a carcinoma for a benign adenoma.

The early diagnosis of these tumors is of great importance regardless of their benign or malignant character, because even if benign they cause bronchial obstruction, with subsequent bronchiectasis, pulmonary abscess or empyema, unless soon removed. The question of malignancy is important, however, both because if malignant some of them would be operable by lobectomy or pneumonectomy, and if benign, the patient could, in most cases, be spared the operative risk and mutilation of these procedures.

*Symptomatology.*—Hemoptysis is perhaps the most common symptom, and for this reason these patients are sent to sanatoria with a diagnosis of tuberculosis. Other symptoms are those of bronchial obstruction, as for example wheezing, productive cough and dyspnea. On physical and X-ray examination, signs of obstructive emphysema or obstructive atelectasis may be found. Many patients present very few symptoms or physical signs in the early stages.

*Bronchoscopic Appearances and Biopsy.*—Benign adenomas, seen through the bronchoscope, generally appear as smooth, rounded,

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\*Presented at the 24th annual meeting of the American Broncho-Esophagological Association, Cleveland, Ohio, June 3, 1941.

reddish tumors in the larger bronchi, projecting into the bronchial lumen, without infiltrating the wall as the malignant tumors do. Sometimes the color is grayish rather than reddish, and not infrequently some blood-stained mucopurulent secretion is present. Bronchoscopic biopsy is generally easy, but as stated above, the histopathologic diagnosis is rather difficult and requires careful study.

*Pathology.*—Some of the cases of adenoma in our series were at first called carcinomas by competent pathologists. One case, which aroused a considerable amount of discussion, was studied by a pathologist who is regarded as a leading authority on neoplastic diseases, and he believed that the tumor would eventually prove itself to be a "peculiar pulmonary cancer." The patient is still perfectly well almost ten years after bronchoscopic removal of the tumor from the left bronchus (Case 6).

While the term bronchial adenoma, now so generally in use, does not seem entirely acceptable in view of the bizarre histology of these tumors, certainly their cellular structure and their apparent incapacity to infiltrate or to metastasize indicate their relatively benign character.

In the typical case of benign adenoma, the surface is generally covered with squamous epithelioma and a wide band of connective tissue is interposed between the surface and the tumor itself. The tumor cells are generally formed in nests, sometimes without any particular arrangement, but more often the peripheral cells are seen to form a definite layer such as is seen in such a characteristic way in basal cell carcinoma of the skin. The more central cells lie loosely without any particular relationship, but sometimes a lumen is seen in the center of these cell nests. The nuclei have the structure of normal or non-neoplastic cells. There is a fine but definite nuclear membrane and a fine distribution of chromatin particles. Mitotic figures are extremely rare.

Incidentally, it is probable that many of the inflammatory tumors, polyps, hemangiomas, fibromas and other benign bronchial tumors are very similar, pathologically and clinically, to the adenomas. Several of our cases were once thought to be tumors of inflammatory origin, but on careful histologic study we have decided to group them with the adenomas. Pollak, Cohen and Gnassi published a case report to which they appended a most interesting review of the literature and tabulation of reported cases. Inflammatory tumors constituted 22% of their cases, but adenomas predominated, consti-

tuting 49%. The entire series comprised 104 cases, 27 diagnosed at autopsy and 77 diagnosed by bronchoscopic biopsy.

*Bronchoscopic Treatment.*—Bronchoscopic treatment of benign bronchial tumors, by forceps removal, implantation of radon seeds, and electrocoagulation has been practiced by a number of bronchoscopists, and is generally successful in maintaining the patency of the bronchial lumen, though often a number of treatments are required. In the more vascular tumors electrocoagulation has a great advantage because it does not precipitate hemorrhage. The current is easily controllable, and should be maintained at a low point sufficient to whiten without charring the surface. A bipolar current is used, the neutral lead being attached to a plate under the patient's back and the active one to the electrode which is passed through the bronchoscope. An ordinary bronchoscope may be used, but there is definite advantage in using a bronchoscope with a special groove for the electrode, as suggested by Kernan, because in this way the shaft of the electrode is held out of the line of vision, and besides, one obtains better control of the electrode.

About five years ago, we reported 12 cases of bronchial tumor before the American Association for Thoracic Surgery. These tumors were tentatively diagnosed as bronchial adenoma, but in the light of subsequent developments and present knowledge, three have now been recognized as low-grade adenocarcinomas, and this diagnosis was proven by autopsy in two of the three. In the future we believe we shall have no difficulty in differentiating low-grade adenocarcinoma from bronchial adenoma because the histopathology is quite distinctive.

Cases 1 to 6 in our previous report<sup>1</sup> have shown by their subsequent course that the diagnosis of benign adenoma was correct. In Case 7 death by asphyxia occurred, and a complete autopsy was performed. Though the pathologist doing the autopsy diagnosed this tumor as mixed tumor of the bronchus, we had, some time before the patient's death, changed our original diagnosis of adenoma to low-grade adenocarcinoma.

Case 8 must be regarded as particularly typical of bronchial adenoma. This patient has enjoyed excellent health and had no recurrence of the tumor. In Case 9 the clinical course was very similar to that in Case 7, and death occurred in a similar way. Autopsy was refused, but many biopsies had been done and they showed a histopathologic picture identical with that in Case 7, which we had

come to recognize as low-grade adenocarcinoma. Cases 10 and 11 are running true to form as typical bronchial adenomas. These patients are still having conservative bronchoscopic treatment at rather long intervals, but are symptomatically well.

Case 12 was the third in which the diagnosis of bronchial adenoma was incorrect. As a matter of fact the original biopsy was reported "adenoma becoming malignant." This patient had a carcinoma of the bronchus with metastasis to the pleura, according to the later clinical diagnosis, which was confirmed by postmortem examination.

Several very interesting additional cases of benign bronchial tumor have been seen since the publication of our previous paper, and one of these cases will be briefly described here.

#### REPORT OF A CASE

L. W., female, aged 19 years, complained of hemoptysis for the past six months, worse in the past three months. She had been given three pneumothorax treatments and a blood transfusion because of hemorrhage.

X-ray on admission showed pneumothorax with complete collapse of the right lung. A series of films brought with the patient showed a gradually developing atelectasis of the right lower lobe, previous to the pneumothorax.

Bronchoscopy showed a grayish tumor mass in the right stem bronchus, from which a specimen was taken for biopsy. A number of bronchoscopies were done for the removal of additional tissue, with a view to relieving bronchial obstruction, and though there was slight bleeding, no serious hemorrhage occurred, and pneumothorax was discontinued. However, it was found impossible to completely eradicate the tumor endoscopically, by forceps and electrocoagulation. In view of this fact and the existence of some cavitation in the lower lobe, it was decided to do a pneumonectomy.

*Course.* Since pneumonectomy was done by Dr. Burnett, about one year after the patient was first seen, she has been symptomatically well. She was able to go through a pregnancy without pulmonary complication, and at present writing it has been two years since pneumonectomy.

*Histology.* Microscopic study showed a very typical bronchial adenoma. Microscopic examination revealed a light-staining fine fibrillar tissue in some places covered on the surface by epithelium but for the most part uncovered. This tissue supported many nests of cells. In each case there was a more or less regular peripheral layer of cuboidal epithelium, and there were scattered epithelial cells more or less completely filling the lumen. The nuclei consisted of a delicate membrane and rather closely packed but tiny, almost ultramicroscopic, chromatin particles. Mitotic figures were not encountered. In some areas these tumor cells were undergoing necrosis with fragmentation and pyknosis of nuclei.

*Comment.* This case is one in which it was felt that, though the tumor was entirely benign, radical operation was justifiable because of the impossibility of eradicating the tumor endoscopically, and more particularly because of the disease in the peripheral portion of the lung.

#### CONCLUSIONS

1. One of the most important groups of bronchial tumors is that constituted by the so-called benign adenomas, which are coming to be widely recognized as a clinical and pathologic entity. It is possible that many of the inflammatory tumors, polyps, hemangiomas and fibromas, in the literature could be classed with the adenomas, pathologically and clinically, as suggested by Womack and Graham.<sup>6</sup>

2. Pathologists who are not especially familiar with these tumors are very prone to mistake them for carcinoma, because while the cellular structure is fairly uniform, it is not comparable to that of benign glandular tumors encountered elsewhere. One must be continually on guard in making the histopathologic diagnosis of a bronchial tumor, because mistakes are easily made both ways.

3. Bronchoscopic treatment is effectual in most cases of benign adenoma and other benign bronchial tumors, but often a number of treatments are required and in some cases it seems impossible to obtain a complete and permanent cure such as will make subsequent treatment unnecessary. In view of the definitely benign character of these tumors and the excellent results obtained by conservative treatment, it would seem that it should be given a trial in every case, but surgical treatment of more radical character, such as lobectomy or pneumonectomy, may be justifiable in some of the cases.

4. Follow-up data is presented in connection with a series of cases previously reported, and one additional case is reported.

255 S. 17TH ST.

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## CII

### BRONCHOGENIC CARCINOMA WITHOUT BRONCHIAL OBSTRUCTION\*

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The importance of bronchial obstruction as an early sign of bronchogenic carcinoma is well established. Upon this clinical manifestation of the disease depend the physical, roentgen, and bronchoscopic findings which enable the diagnosis to be made early enough to permit live-saving surgery. The purpose of this paper is to present three cases of malignant bronchogenic neoplasms which gradually infiltrated both lungs to produce death without evidence of bronchial obstruction or pulmonary suppuration.

#### REPORT OF CASES

Mrs. L. S., 49 years of age, was admitted to St. Luke's Hospital on August 8, 1939, for diagnostic studies to determine the cause of her irritating nonproductive cough. She had been perfectly well until eight months previously, December, 1938, when the attacks of coughing began. They were especially annoying at night, recurring in paroxysms lasting several minutes, and were nonproductive. Only very occasionally did the patient raise a small quantity of tenacious mucus. There had been no weight lost, chest pain, wheeze, or hemoptysis. Her temperature at the time of admission was 98°, pulse, 84, respiratory rate, 24, and her blood pressure, 90/60. A careful physical examination on admission to the hospital showed practically no positive findings to which her pulmonary complaint could be attributed beside a slight suppression of breath sounds in the left apex. The roentgen examination revealed a diffuse infiltration extending outward from the left hilum into the upper

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Presented before the 24th annual meeting of the American Broncho-Esophagological Association, Cleveland, Ohio, June 3, 1941.

left lobe with several areas of increased density located in the left hilus which were reported as possibly due to enlarged hilar glands. A bronchoscopic examination was made August 9, 1939. The motility of the larynx was normal; the mucosa of the trachea and the right bronchus were essentially normal. That of the left side was slightly inflamed and somewhat thickened. Although all the bronchial orifices were patent on the left side it was thought that possibly there was a slight narrowing of the lumina of these bronchi. Practically no secretion was found in the left bronchus, but the slight amount present was aspirated for stains and culture; no organisms were found, nor did any grow on the usual culture media. A bronchogram was made August 10, 1939. Iodized oil entered the left lower lobe easily and outlined all the bronchial divisions. The oil entered the major bronchi of the left upper lobe, but while there was no definite interruption in the branches visualized by the oil, the oil failed to enter the smaller bronchi and bronchioles of the left upper lobe. The patient's temperature, pulse and respiration were normal during her hospital stay. On August 21, 1939, re-examination of the chest roentgenologically showed some improvement with an apparent decrease in the infiltration of the left upper lobe over previous examinations. On October 3, 1939, further improvement in the left apex was noted, roentgenologically, but an extension of the process downward along the lower portion of the left upper lobe was found. Examination December 6, 1939, showed an increase in the infiltrative process of the left upper lobe. No atelectasis was present, but the hilar shadows on both sides had increased. The patient was admitted to the hospital at this time for a second bronchoscopic examination. She had been well, had gained weight, and had had a normal or subnormal temperature, but her nonproductive coughing paroxysms had persisted. A frothy, blood-tinged sputum was noted for the first time on the day of her admission to the hospital. A dull pain in her left side, which was made worse on coughing, had been present for two or three weeks. Physical examination showed equal expansion of the two sides with a decrease of vocal fremitus over the anterior chest wall. There was a decrease in resonance over this same area and the breath sounds were diminished. A bronchoscopic examination made December 15, 1939, showed a normal tracheobronchial tree except for an inflammatory appearance of the left upper lobe bronchial orifice. Small pieces of tissue removed from this area merely showed an inflammatory bronchial mucosa without evidence of neoplasm. Smears and cultures made of the bronchoscopic sponges used to wipe the upper lobe orifice were sterile except for one small colony of *Aspergillus*.

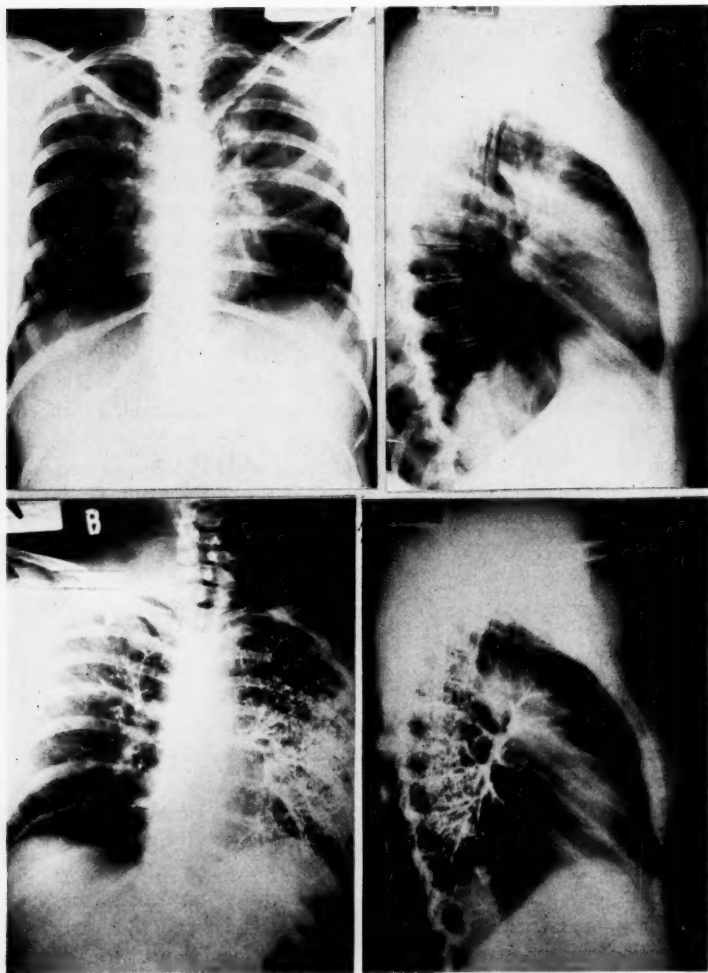


Fig. 1, Case 1. Postero-anterior and lateral roentgenograms and bronchograms of the chest of a 49-year-old, white female whose chief complaint was paroxysms of unproductive cough of eight months' duration. Note the hazy infiltration of the upper lobe of the left lung and the elevation of the left diaphragm. The left bronchus was entirely patent. In the bronchogram the left lower lobe is seen to fill completely. Oil fails to run into the smaller divisions of the left upper lobe bronchi, but the major bronchi are patent.

Iodides were administered in large doses because of this finding, but the possibility that the single colony might have been a contaminant, or of no pathogenic significance, was considered. A bronchogram at this time again showed that the bronchi were patent, but the oil did not extend into the periphery of the left upper lobe. The temperature, pulse, respiration and sedimentation rate were all normal during the hospital stay. Many examinations for tubercle bacilli and guinea pig inoculations were made, but these were consistently negative.

The patient definitely improved following the bronchoscopic examination and the iodide therapy. She was in Arizona during the winter but toward spring again complained of her original symptoms and although she was up and about was gradually becoming somewhat short of breath. At this time the patient coughed up a piece of red darning cotton and it was recalled that she had mentioned that she had frequently placed darning cotton in her mouth while she was sewing and might have aspirated a piece of it. The piece of cotton which she exhibited was so large it could only have been in one of the major bronchi had it been present throughout the duration of her symptoms and responsible for them; but no evidence of a foreign body had been noted during the bronchoscopic examinations. During the late spring and summer of 1940, symptoms progressed rapidly with an increasingly productive cough, loss of weight, chest pain and dyspnea. X-rays showed an increasingly bizarre picture of distortion of the left diaphragm, advancing infiltration into the left lower lobe and a gradually advancing infiltration in the entire right lung. During the few weeks prior to death the left pleural cavity contained an increasing amount of fluid. At no time was there any evidence of a bronchial obstruction. Terminally she obtained relief only with a helium-oxygen mixture. She expired on August 7, 1940, just one year after the original hospitalization.

Postmortem findings are herein limited to positive findings although a complete examination was made. It showed both lungs to be completely involved in an extensive neoplastic process. The left upper lobe was hard, nodular, noncrepitant, markedly shrunken, and compressed toward the midline. The remainder of the lung had a firm, rubbery consistency and few air-containing areas. The right lung was likewise firm in consistency but not to as marked a degree as the left. The external surfaces of the lungs were glistening, black or slate-grey, focally nodular or corrugated. The surfaces made by cutting were basically slate-grey with pin-head sized, grey-white dots and a mesh of grey-white streaks. Surfaces made by cutting

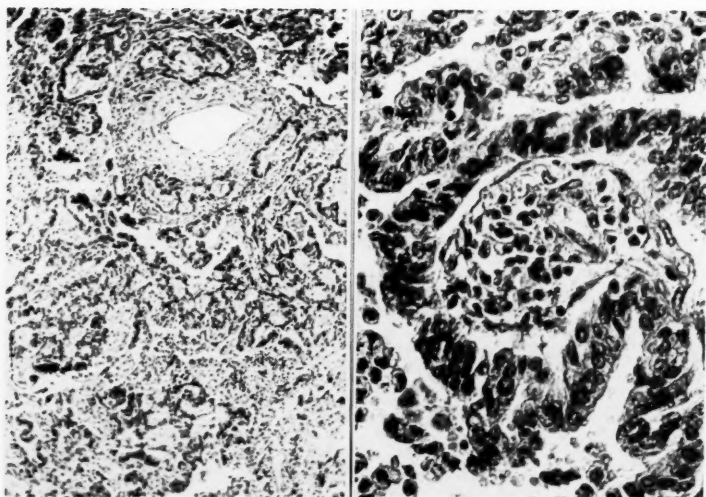


Fig. 2, Case 1. Photomicrograph of adenocarcinoma arising in the bronchioles of the upper lobe of the left lung. The carcinoma extended throughout both lungs by way of the peribronchial and perivascular lymphatics. At no point did it erode through the mucosa.

parts of the right lung were pinkish and glistening, but punctate white dots were seen throughout. Examination of the bronchi showed them to be patent throughout and somewhat dilated in their peripheral ramifications. The mucosa was moist and velvety and without a demonstrable break. The microscopic examination of the tissues removed showed an alveolar carcinoma of the lung arising in the bronchioles of the left upper lobe. Metastases were found extending to the left lower lobe, the right lung, the tracheo-bronchial, periesophageal and cervical lymph nodes, and to the musculature of the stomach. Sections from the left upper lobe consisted largely of epithelial cells which had assumed an alveolar pattern, in many sections being imposed on the lung framework. Dilated alveoli were seen to be lined by single-layered low cuboidal cells which gradually fused with cylindrical cells, forming intra-alveolar projections. The cells had round or oval vesicular nuclei which varied somewhat in chromatin content and occasional cells had mitotic figures. The mucosa of the bronchi was often desquamated but showed no neoplastic variation. The arteries were markedly thickened, and in the perivascular lymphatics were tumor cells in

adenomatous formation. Sections through all the other lobes revealed the neoplastic cells, in adenomatous formation and within the vascular channels. Thus, the patient had an adenocarcinoma arising in the bronchioles of the left upper lobe of the lung. The carcinoma extended throughout both lungs by an invasion of the peribronchial and perivascular lymphatics, but nowhere did it erode through the mucosa to give localized intrabronchial evidence of its presence.

The second case is that of a 62 year old white male, W.H., who entered St. Luke's Hospital on October 10, 1938, complaining of a severe cough of seven months' duration and a loss of weight during the past three months. The cough was entirely nonproductive and paroxysms were severe enough to give him frequent headaches. He gave no history of a previous respiratory infection, had had no hemoptysis, loss of weight or fatigue. The temperature, pulse and respirations were normal, and the physical examination showed a well-developed, well-nourished white male who apparently was not very ill. The only positive findings in the examination were an injected pharynx and an almost complete absence of the nasal septum. He had had an operation on his nose many years previously. The chest examination was essentially negative except for a slightly enlarged heart. The laboratory data were within normal limits. The Wassermann test was negative and sputum examinations were consistently negative for acid-fast organisms. The roentgen examination of the chest was surprising in view of the almost complete absence of physical findings. Both lungs had a diffuse, flaky appearance which was about equally prominent on the two sides. The heart shadow was rather indistinct because of the pulmonary pathology. The costophrenic angles were clear, and while the left diaphragm was normal the right was slightly irregular. With this picture in mind, the patient was carefully questioned regarding his occupation, and no occupational association could be made. He had not been a miner, he had not worked with silica or glass nor in asbestos. A bronchoscopic examination made on October 11, 1938, showed a relatively normal tracheobronchial tree without evidence of a tumor or an inflammatory process. A slight amount of secretion was removed for bacteriologic examination and a light growth of micrococci and diphtheroids was obtained, as well as frequent colonies of a yeast. When these were subcultured for identification they were found to be *Monilia*. These findings were consistent with the roentgen findings, and large doses of iodides were administered. A month later the patient was readmitted to the hospital. His cough was more persistent and quite productive,



Fig. 3, Case 2. A—Diffuse, flaky appearance of both lungs of a 62-year-old white male complaining of cough and weight loss. B—Marked increase in the process after seven weeks. Bronchoscopy had been negative except for the isolation of *Aspergillus*. Postmortem revealed an indurative extramural bronchogenic carcinoma.

and he had had pains throughout both sides of the chest. Physical examination at this time showed a paralysis of the right vocal cord, evident loss of weight, and a considerable diminution of the resonance and the breath sounds throughout the chest. The roentgen examination showed a marked limitation of motion of both sides of the diaphragm and an increase in the diffuse, flaky process which extended throughout both lung fields, especially on the right. There was no change in the bronchoscopic appearance. The tracheobronchial tree appeared to be essentially normal in spite of the roentgen evidence of an advanced pulmonary process. During the succeeding month the patient became dyspneic and finally orthopneic, and he was readmitted to the hospital December 28, 1938. A serious respiratory and cardiovascular decompensation was present and he was given oxygen therapy and cardiac stimulants. At this time a skin sensitization test was positive for *Monilia* infection. His condition grew worse rapidly, and he expired January 4, 1939.

The postmortem examination showed a marked hyperemia of the lining of the trachea and bronchi. Beginning at the bifurcation



of the trachea it was found to be encroached upon by a mass of hard tissue just above the bifurcation, which was 3.5 cm. wide and 3 cm. dorsoventrally. This mass was closely attached to the trachea, and the edematous lining opposite had a number of small pit-like depressions. There was a slight hyperemia but no ulceration of the lining at this level. The examination of the divisions of the right bronchus disclosed the air passages with their usual longitudinal folds. The lining of the upper part of the trachea was grey and smooth. The pleura of both lungs was dark grey, mottled with carbon and covered extensively with single and confluent grey nodules ranging to 1 cm. in diameter. On surfaces made by cutting there were single and confluent grey nodules. The main bronchi, opened to their smaller divisions, had smooth linings. Sections from the tumor tissues of the trachea had a moderately dense, mesh-like fibrous stroma. These stroma tissues were markedly ingrown by small cords of large acidophilic epithelial cells arranged in mosaics. The growth of epithelium was widespread through the sections and many of the cells were in mitosis. There were no duct or glandular structures, but rather the epithelium was arranged in short cords, one to two cells in width. The stroma tissues had small numbers of lymphocytes and mononuclear cells. No normal epithelium was present. The pleura of the lung was markedly thickened by dense fibrous tissue widely ingrown by cords of epithelial cells similar to those described in the trachea. The tumor tissues penetrated the pleura and invaded the pulmonary tissue. In many regions the epithelium was arranged in large duct-like structures, and the epithelium was in papillary folds. There were many cells in mitosis. The carcinoma tissues were also present in the perivascular and peribronchial lymphatics. In contrast to the epithelial cells in the trachea, these cells were basophilic. The tracheobronchial lymph nodes were almost completely replaced by a dense fibrous stroma widely ingrown by cords of epithelial cells, arranged in mosaics and in large duct-like structures; many were in mitosis. Thus, the postmortem examination showed an indurative extramural bronchogenic carcinoma of the right lung with extensive metastatic carcinoma of both lungs. Metastases to the right and left parietal and visceral pleura, and to the tracheobronchial lymph nodes, were found. There were no metastases to other parts of the body.

The third patient, L. F. R., a 49 year old white male, a dentist, was admitted to St. Luke's Hospital December 8, 1940, complaining of a dry cough of two and a half months' duration, a weight loss of 22 pounds in the last three months, malaise, loss of appetite, and slight hoarseness. The patient stated he had felt well until

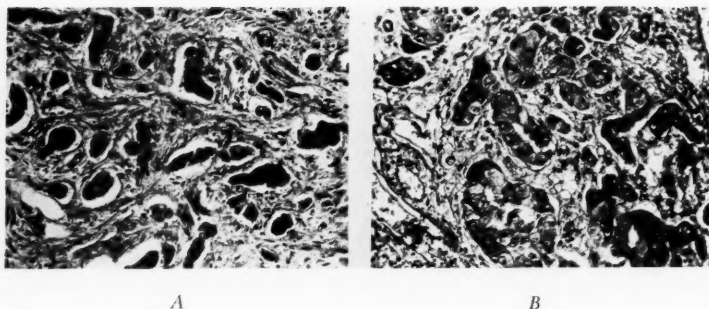


Fig. 4, Case 2. A—Photomicrograph of the tissue in the primary bronchogenic carcinoma. B—Photomicrograph illustrating the structure of the bronchogenic carcinoma metastatic in the parabronchial lymph nodes. (X198—Both A and B.)

September 20, 1940, when, following a cold, he developed a dry cough which seemed to be worse during the night. Paroxysms of cough increased in frequency and duration and, as in the first case, were always worse at night. The cough was not productive except that occasionally a small amount of clear, viscid mucus was raised. While there was no pain in the chest, the patient complained of some soreness throughout, probably due to excessive coughing. His temperature on admission to the hospital was 98.2°, pulse, 92, respiratory rate, 18, and his blood pressure, 117/80. He was well-developed, rather poorly nourished, alert and cooperative. His red blood count was 5,670,000, and his hemoglobin, 17 gm. per 100 cc. His white cell count was 15,800 of which 72% were neutrophils, 24% lymphocytes, and 4% were eosinophils. Examination of the chest revealed a limited expansion of the left lung, an absence of tactile fremitus above the left base, diminished breath sounds at the left base, and highly variable, wheezing, distant, musical rales in the left lung field. Similar wheezing rales were found on the right side but to a much lesser degree. The remainder of the physical examination, as well as the laboratory examinations, which included sputum examinations for tubercle bacilli, tumor cells and fungi, showed no findings significant to the present illness. The roentgen examination showed increase in the hilar shadows on both sides with a diffuse, infiltrative process extending outward into the parenchyma

of both lungs. This process was most marked in the left lower lobe, and it had extended considerably on both sides from the apparent degree of involvement noted on roentgen films taken October 25, 1940. A bronchoscopic examination, made December 9, 1940, showed the larynx to be grossly normal, the tracheal mucosa to be somewhat reddened, and the carina, thin and sharp. The remainder of the examination was essentially negative. A small amount of secretion was aspirated for culture. Following the bronchoscopy, the patient had a definite change in symptomatology. Large quantities of mucopurulent material were coughed up, but the bacteriological studies showed no significant findings. The patient's temperature, pulse and respiration were normal during his hospital stay. The patient was somewhat improved temporarily and he stated he could breathe more easily after raising large quantities of mucopurulent material on cough following the bronchoscopy. This averaged eight ounces per day and for the first time was occasionally streaked with blood. Following a brief improvement, the patient became dyspneic and gradually weaker. Many rales were found throughout both sides of the chest, bubbling in character. He was re-admitted to the hospital December 22, 1940, and X-rays revealed a definite increase in the infiltrative process which extended throughout both lungs. A second bronchoscopic examination was made December 23, 1940, and showed the configuration of the tracheobronchial tree to be similar to that of the previous examination. All bronchial orifices were patent and the appearance of the mucosa was similar to that noted previously. Secretion was again aspirated for staining and culture. These examinations showed no significant findings. The patient's course was rapidly downhill, and he developed an increasing amount of fluid in the right pleural cavity. This was aspirated on December 31, 1940, and the sediment fixed and examined histologically. A few aggregated masses of cells in the form of mosaics were found and considered to be metastatic carcinoma. The patient's respiration gradually became more difficult and within the next few days oxygen, and helium and oxygen, were used to alleviate his respiratory symptoms. He expired on January 4, 1941.

The postmortem examination showed a bilateral, diffusely infiltrative bronchogenic "signet cell" carcinoma of the lung with carcinoma metastases to the thymic body, the tracheobronchial and mesenteric lymph nodes, the mediastinal tissues, the ribs, and the vertebrae. The visceral pleura of the left lung was thick, grey-white, rough and granular. The broad surfaces of the lung made

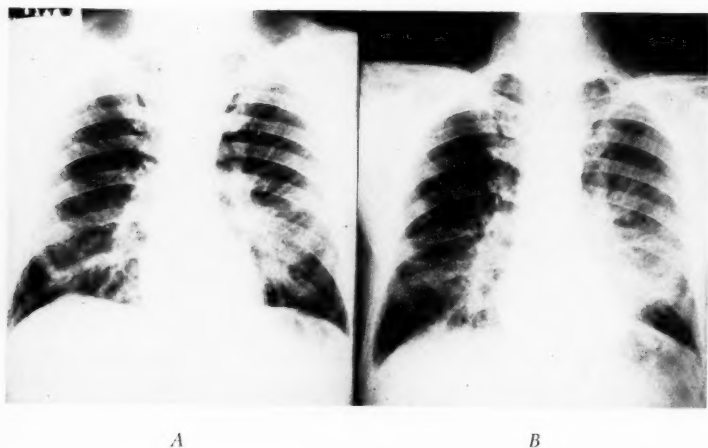


Fig. 5, Case 3. *A*—A chest roentgenogram of a 49-year-old white male who had had paroxysms of cough for one month. Note the perivascular and peribronchial infiltration extending toward the periphery of both lungs, most markedly into the left upper lobe. *B*—Increase in prominence of all markings five weeks later.

by cutting revealed a grey-pink tissue with prominent septa studded with small, grey, nodular lesions which were thickened bronchioles. The bronchi were intensely hyperemic and there was no occlusion of the lumina of the bronchi traced to their finer divisions. Their walls were thick, hard, white and glistening, had lost their longitudinal folds and ranged in thickness between 3 and 7 mm. There were no tumor nodules in the lining of the trachea or bronchi. Microscopic sections of the lung showed the alveolar septa to be thin and the alveoli themselves relatively free of exudate although there were occasional erythrocytes, desquamated epithelial cells and large mononuclear phagocytic cells present. The lymphatics accompanying the smaller bronchi and the pulmonary blood vessels were dilated and contained masses of carcinoma cells. These were medium in size, round, and had a pale, vacuolated cytoplasm with compressed peripheral nuclei, some of which were in mitosis. Many of the cells looked like signet rings. Fibrous tissue about the lymphatics was increased and infiltrated by lymphocytes and plasma cells. The carcinoma cells appeared to be confined to the lymphatics about the smaller bronchi.

## DISCUSSION

A number of points of similarity existing in these three cases establish them as a type of bronchogenic carcinoma which, from a clinical standpoint, presents unusual diagnostic problems. The recognized criteria in the symptomatology, roentgen examination and bronchoscopic appearance, generally used in establishing the diagnosis of the disease are uniformly absent in these three cases. A study of the three patients at the time of their first admission to the hospital shows that of all the symptoms usually found in early bronchogenic carcinoma, only a persistent cough was found in each case. The accompanying chart compares the symptoms in the three cases at the time of their first admission to the hospital.

TABLE I  
COMPARISON OF SYMPTOMS AT TIME OF FIRST ADMISSION  
TO THE HOSPITAL

SYMPTOM	CASE 1 L. S.	CASE 2 W. H.	CASE 3 L. R.
Duration of Symptoms	8 months	7 months	3 months
Cough	Yes	Yes	Yes
Productive?	No	No	No
Weight Loss	No	Yes	Yes
Wheeze	No	No	No
Chest Pain	No	Yes	No
Dyspnea	No	No	No
Hoarseness	No	Yes	Yes
Malaise	No	Yes	Yes
Fever	No	No	No
Hemoptysis	No	No	No
Loss of Appetite	No	Yes	Yes

A study of the roentgen findings of these three cases likewise fails to show consistent pathology upon which the diagnosis of the disease could be established. As a matter of fact, the roentgenograms of one of the patients (Case 2) are so characteristic of the lesions produced by a fungus disease that this diagnosis was made without question from the films. The roentgenograms of the other two patients were not inconsistent with those of a fungus disease and consequently did not definitely eliminate fungus disease of the lungs as a diagnostic possibility. The actual isolation of fungi from the bronchoscopically-obtained sputum further confused the diagnostic problems.



Fig. 6, Case 3. (a) Carcinomatous infiltration of the bronchial wall and invasion of a peribronchial channel.

A—Bronchial lumen.

B—Bronchial wall.

C—Lymphatic channel invaded by tumor cells.

(b) Photograph of a surface made by hemisecting the inflated formalin-fixed right lung (peripheral half). Note the marked fibrous thickening of the bronchial walls. Masses of tumor cells had spread along the peribronchial lymphatics, as illustrated in the photomicrograph (a).

Of greatest significance is the histological examination of the lungs. The metastatic spread of the carcinoma cells throughout both lungs was a lymphatic one in each case. The small primary lesion was difficult to establish in two of the cases (1 and 3) and relatively large but entirely extra-bronchial in the third (Case 2).

Distant metastases from minute, silent bronchogenic carcinomas producing extensive, severe, and eventually fatal complications have been responsible for many perplexing diagnostic problems. This type of bronchogenic carcinoma is not uncommon. Seyfarth<sup>1</sup> described these small bronchogenic carcinomas as soft, warty thickenings of the mucosa, but stated they were associated with a polypoid constriction of the bronchial lumen. Kikuth,<sup>2</sup> however, described them as merely rough thickenings of the bronchial lining, scarcely elevated and as small as 3 sq. mm. He stressed the fact that they involved the entire bronchial wall. Similar to the cases herein presented, he described a marked infiltration of the lymphatics of one lobe of the lung with a somewhat more diffuse lymphatic infiltration of the entire lung. Metastases to the bones often occurred in these cases to overshadow completely the pulmonary symptomatology, or prove fatal without evidence of pulmonary symptoms. Thomas, Hirsch and Blaine<sup>3</sup> report a case with unusual bone changes caused by the metastases of a small primary bronchogenic carcinoma which gave no pulmonary symptoms and was not found until the examination of the lungs was completed some time after the post-mortem examination. Twining<sup>4</sup> mentions the small, flat tumors that may spread in the submucosa without alteration of the lumen of the bronchi, but states that the rapid spread into the parenchyma of the lung along the peribronchial lymph vessels follows a perforation of the bronchial wall.

Thus, the small, relatively silent bronchogenic carcinomas are recognized eventually either because they break through the bronchial walls, or because they lead to the death of the patient through their extremely extensive distant metastases. The cases herein described differ from these two groups in that while the primary lesions were silent, the metastases to other parts of the body were unimportant. Furthermore, the spread of the disease in each case took place by an invasion of the peribronchial and perivascular lymphatics without erosion of the bronchial walls.

In an effort to establish an antemortem diagnosis in these cases, few procedures are available. Bronchoscopically the direct removal of tissue from the bronchial wall might have given positive histo-

logic evidence of the carcinomatous nature of the lesions. However, it is generally considered inadvisable to penetrate what is apparently a smooth mucosal wall. The withdrawal of fluid from the pleural effusion in Case 3 demonstrated the importance of the histologic examination of the sediment of this fluid. The diagnosis was established antemortem in this case through this examination because the structure of cell groups could be demonstrated. Fixation and sectioning of this sediment is thus superior to staining simple smears because of the destruction of this cellular relationship which accompanies the latter procedure.

Needle biopsy and exploratory thoracotomy must also be mentioned in discussing the diagnostic procedures available to these patients. However, since it was characteristic of these three cases that marked hilar infiltration was present in each at the time of their first roentgen examination, the positive evidence that these procedures might have given would have been obtained when radical surgical extirpation of the lesion would have been impossible.

#### SUMMARY

Three cases of bronchogenic carcinoma are presented in detail that are characterized by extensive carcinomatous invasion of both lungs without bronchial obstruction. The similarity in the unusual gross and microscopic characteristics and clinical manifestations accounts for their being considered a special group.

We are indebted to Dr. Edwin F. Hirsch of St. Luke's Hospital for the post-mortem examinations of Cases 2 and 3, and to Dr. Otto Saphir of Michael Reese Hospital for the postmortem examination of Case 1.

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## Notice

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### CASSELBERRY AWARD

The American Laryngological Association has now available a sufficient sum of money to be granted as a prize for a thesis dealing with original investigation and research in the art and science of laryngology and rhinology. Theses or reports of work must be in the hands of the Secretary before March 1, 1942.

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